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## Original Communications

### EXPERIMENTAL STUDIES ON THE TOXEMIAS OF PREGNANCY\*

CAN HISTAMINE POISONING BE REGARDED AS THE ETIOLOGIC FACTOR?

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#### I

UPON no problem in obstetrics has so much effort been expended as in attempts to elucidate the cause of the toxemias of pregnancy. Yet our insight into this field today is based upon but little more fundamental knowledge than it was two decades ago. The extensive chemical studies which have been made in recent years have thus far failed to afford an acceptable explanation for the basic phenomena. They have reflected the results of derangements which occur in various organs, but they have not thrown light upon the etiologic antecedents. There need be little wonder, therefore, that on several occasions it has been suggested that we should hesitate to discuss the existence of toxemias of pregnancy until the toxic agents concerned in their production have actually been demonstrated. "Toxemia is often a shibboleth of the profession. When a disease cannot be diagnosed, it is put down as a toxemia. This, however, is not medical science—it is medical shirking" (Macleod).

The work done during the last few years on the problems under consideration shows a tendency to consider their fundamental phenomena as beginning in the realm of physiology and ending in that of pathology. Thus, recent investigations tend to stress the problems

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of the normal and of the abnormal by widening, as comprehensively as possible, our present state of knowledge of the biology of pregnancy, particularly with regard to alterations in the liver function, the action of the ductless glands and their intimate relations with the vegetative nervous system. The numerous articles dealing with development of edema in various areas of the pregnant organism and with demonstrable changes in the behavior of the capillaries offer a good example of the progress in this field, which is concerned with physicochemical subtleties. But, there is a consensus of opinion that in the investigation of a problem of this nature, little real progress as to basic phenomena can be made until it is possible, either to identify positively the causative toxic substances or to reproduce in experimental animals the characteristic clinical syndromes, as well as the microscopic and chemical features of the toxemias of pregnancy.

The writer has chosen the latter mode of approach, and in the present study will give a brief report of the results obtained in several series of experiments and will offer such conclusions and applications as are based upon his observations, particularly as regards the clinical phenomena which occur in severe cases of *premature separation of the placenta, pernicious vomiting, and eclampsia*. "The ultimate object of all medical research is practice. In the final analysis the test of the value of any research is to be found in the application of the results" (Patterson). While the experiments were first undertaken in the hope of producing premature separation of the placenta in laboratory animals by the intravenous administration of histamine, for reasons referred to later it soon became apparent, after we had become acquainted with the notable structural changes in the liver and kidney resulting from the employment of this substance, that a number of additional investigations concerning other toxemias might be profitably undertaken by changing the experimental conditions. The animal experiments were conducted in the Pharmacological Department of the Johns Hopkins University, where I had the privilege of working with Dr. E. M. K. Geiling; the subsequent microscopic studies of the organs were made in the Obstetrical Laboratory. A preliminary communication dealing with the first part of our experiments, which were performed during May and June, 1925, was published in the February number of the Johns Hopkins Bulletin for 1926.

My special interest in histamine as a possible causative toxic factor in the production of premature separation of the placenta, was aroused by the microscopic study of sections obtained from uteri which were removed at operation or autopsy from women presenting that condition. As Williams points out in his recent paper, the lesions consist in intramuscular hemorrhage which leads to disassociation of the muscle fibers, and which is due to damage to the walls of veins of

small and moderate caliber; while outside of the hemorrhagic areas the muscular fibers are spread apart by edema. When the tubes and ovaries and broad ligaments are involved the hemorrhagic infiltration can be traced in places to similar changes in the periphery of small veins. These findings appeared to me to be indicative of the action of a poisonous substance which affects the vessels by making their walls permeable for plasma and corpuscles. Furthermore, upon taking into consideration the shock which develops in severe cases and which is frequently out of all proportion to the amount of blood lost, the picture of experimental histamine intoxication was called to mind.

In the attempt to reproduce premature separation of placenta by a mechanism similar to that observed in human beings, pregnant guinea pigs were chosen on account of the fact that placentation in that

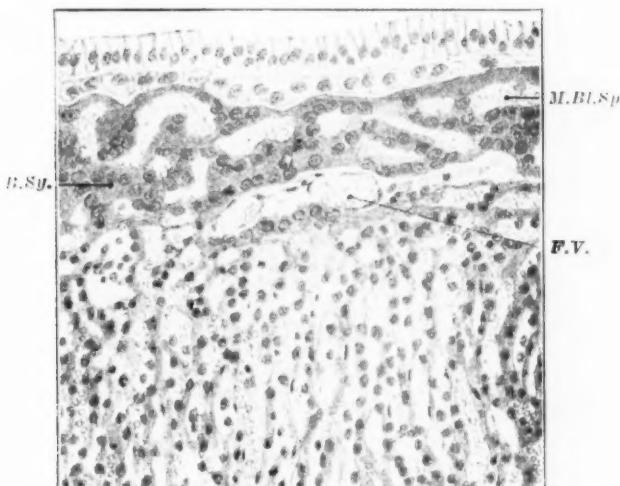


Fig. 1.—Section through margin of normal guinea pig placenta (Grosser). *F.V.*, fetal vessel; *B.Sy.*, border syncytium; *M.BLSp.*, maternal blood space.

species exhibits a reasonable likeness to that of human beings, particularly in that the cotyledon is attached to the periphery—ectodermal giant cells and ectoplacental entoderm—by plasmoidal roots suggestive of the fastening villi in the human placenta. Since the syncytial columns give rise to a meshwork containing maternal blood, they present a functional similarity to the intervillous spaces in the human placenta (Fig. 1).

The experiments were conducted upon 14 pregnant guinea pigs, most of them being in the last week, and only a few in the first half of pregnancy. No anesthetic was employed. Histamine was given intracardially in doses of 0.25 to 1.0 c.c. of a 1 to 1,000 solution per kg. of body weight, one to three injections being given at intervals of an hour. In those instances, in which repeated injections were given, the initial dose never exceeded 0.25 c.c. per kg. A marked difference in the sensitiveness of the animals toward histamine could be noted, and the degree of

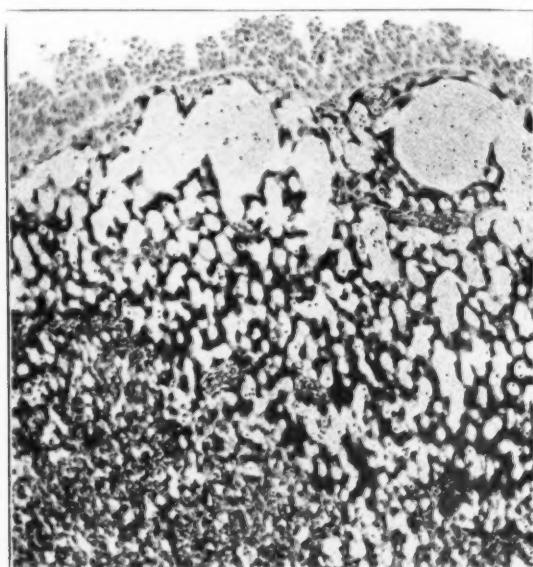


Fig. 2.—Section through margin of guinea pig placenta after injection of histamine, showing damage to fetal septa, and distention of maternal blood spaces (end of four weeks).

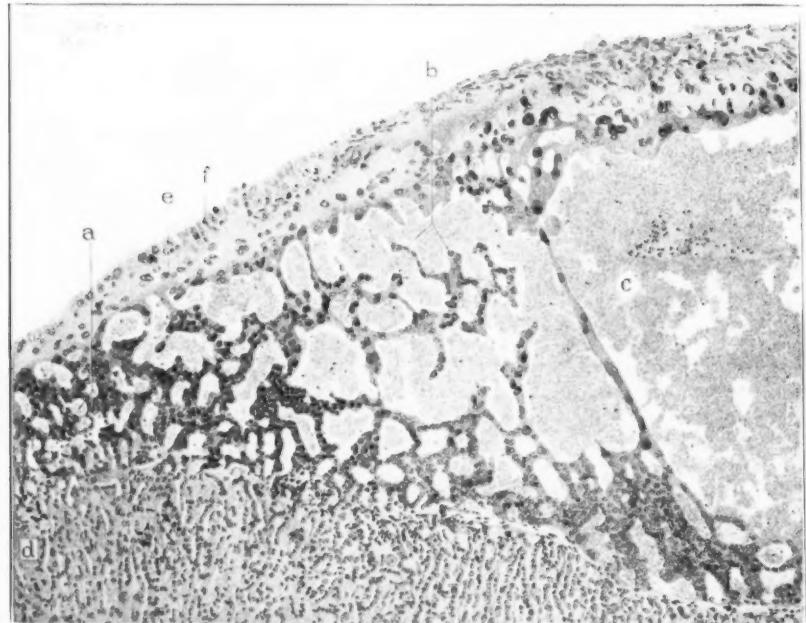


Fig. 3.—Same as Fig. 2, except at term, showing greater damage to tissue and greater distention. *a*., syncytial blood spaces; *b*., ectodermal giant cells; *c*., ruptured syncytial septa; *d*., free hemorrhage after extensive rupture of syncytial septa.

shock produced by the same dose varied greatly. The abdominal organs were removed after the animals had recovered from shock and were immediately hardened in 10 per cent formalin, and a few days later, cross sections through the pregnant uteri were made. The microscopic examination of the pregnant organ showed a striking picture; the invariable result in guinea pigs was that in different places the fastening plasmoidal roots had become detached to a greater or less extent, and that the placenta had been in part separated from its basal tissue by hemorrhages. Thus, in various specimens, almost the entire basal area of a cotyledon lies free, and upon closer examination, it can be seen that the maternal blood spaces at its basis, which, as described above, normally present a dainty meshwork of plasmoidal rootlets, had become dilated ad maximum. Since the delicate syncytial columns were unable to withstand the sudden increase in tension exerted by the enormous and paroxysmal dilatation of the maternal blood spaces, they were torn asunder or were broken off, and the previous normal connection between the cotyledon and the underlying tissue was interrupted. This mechanism becomes apparent by demonstrating that the free ends of the torn plasmoidal roots, while still attached at one side, are floating in the effused blood. Since the same phenomenon has taken place in the maternal veins, which run in the connective tissue septa between adjacent cotyledons, their mutual connection is occasionally severed by hemorrhage or by enormously dilated, thin vessels (Figs. 2 and 3).

Occasionally, even in the area of a single cotyledon, a hyperdistention of maternal veins may lead to a local hemorrhage. Likewise, a striking dilatation of the capillaries and veins is noted throughout the entire generative tract, and in addition it is noteworthy that hyalin thrombi can be seen within the vessels in the uterine wall. Actual hemorrhage, however, only occurs in the areas in which the tissues in the neighborhood of maternal blood spaces are exceedingly delicate, as, for instance, at the base of the cotyledon. Similar conditions, likewise, account for the occurrence of widespread hemorrhage within the chorionic tissue in the placenta of carnivora.

Six additional experiments were performed in order to obtain information as to whether the action of histamine in the conditions under consideration may or may not be regarded as specific. By way of control, histamine-free peptone, pituitrin and adrenalin were administered intravenously to three groups of two guinea pigs, respectively, but in none of them did the placenta show any material deviation from the normal.

Since our studies aimed primarily to solve the problem of premature separation of the placenta, the injections of histamine were made in those species of animals whose placentation simulates to some extent that of human beings, and which in addition, are sensitive toward histamine. Pregnant monkeys, of course, would have been the ideal animals for experimentation; but since they could not be procured it was deemed wise to select guinea pigs for our experiments. Rats could not be employed, as they are not at all sensitive toward histamine. Nor could one expect to produce premature separation in carnivora by the same mechanism as in human beings, on account of the *labyrinthine* structure of their placentae, and particularly since the relations of the decidua and decidual vessels differ altogether from those obtaining in man—a point which is of decisive character, as will be shown later.

On the other hand, the immediate incentive to an investigation concerning the effect of histamine upon pregnant dogs and cats was supplied by the statements of Simonds, Mauthner and Piek, that,

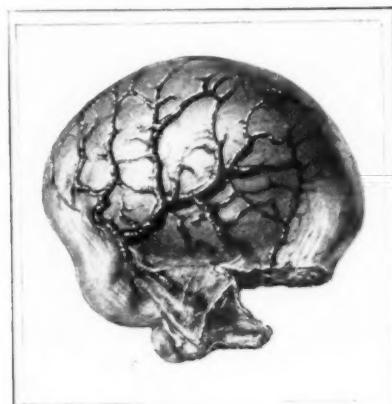


Fig. 4.—Uterine horn of pregnant cat immediately after injection of histamine, showing marked distention of maternal vessels.



Fig. 5.—Human uterus removed on account of premature separation of placenta, showing distention of vessels and hemorrhagic lesions of uterine wall, and appendages (Williams).

owing to the fact that the hepatic veins in carnivora are especially rich in smooth muscle, there is a marked response toward histamine and peptone, as shown by the complete occlusion of efferent veins and

the temporary blocking of the escape of blood from the liver. Furthermore, it was felt that the direct observation of the processes occurring on the surface of the uterus and its appendages following

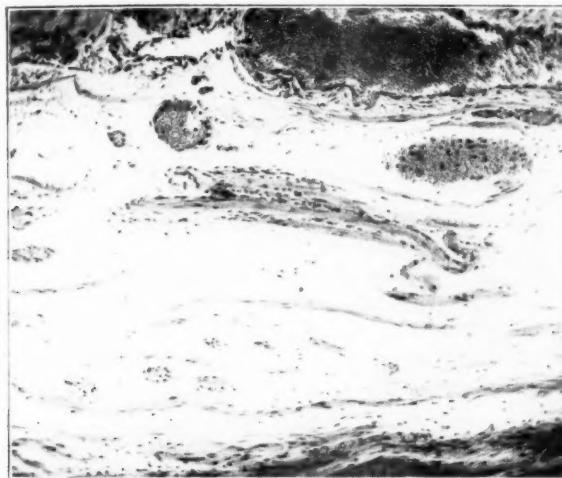


Fig. 6.—Section through wall of cat's uterus, showing separation of muscle fibers by edema. Note presence of clasmatocytes.

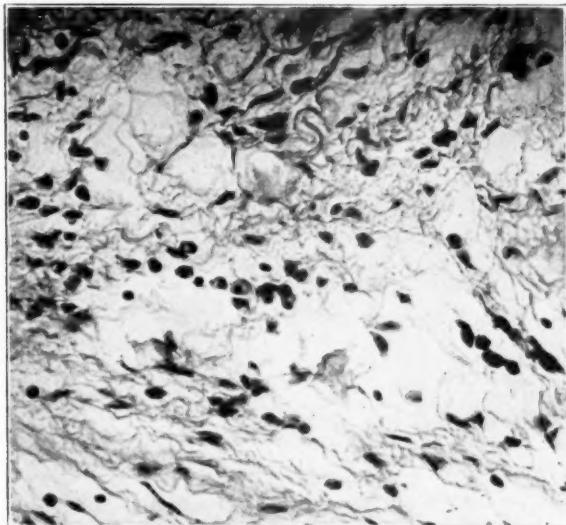


Fig. 6-A.—Higher magnification, showing throngs of clasmatocytes.

the intravenous injection of histamine, would in all probability be more striking in larger animals. For this reason, a typical experiment of this group will be described.

A cat, in the second half of pregnancy, weight 2 kg., chloralose anesthesia intravenously. Ten minutes later the lower part of the abdominal cavity was opened

quickly, and the animal was kept in a warm water-bath. Then 1 c.c. of a 1-1,000 histamine solution was given intravenously. The uterus went immediately into tetanic contraction, and even the smallest venules on its surface became visible, while the larger vessels, as well as those of the broad ligament, became immensely engorged. At the same time, the animal passed into a condition of shock with a marked fall in blood pressure, from which it recovered after eight minutes. Thirty minutes after the first injection, a second dose of histamine twice as large as the first dose was given. In addition to the marked dilatation of the vessels, a number of purplish spots appeared at the ends of the several segments of the uterine horns. These spots did not disappear when the animal was sacrificed in good condition ten minutes later.

Fig. 4 illustrates the findings after the first injection of histamine. The uterine vessels are seen to be engorged with blood and present a picture similar to that

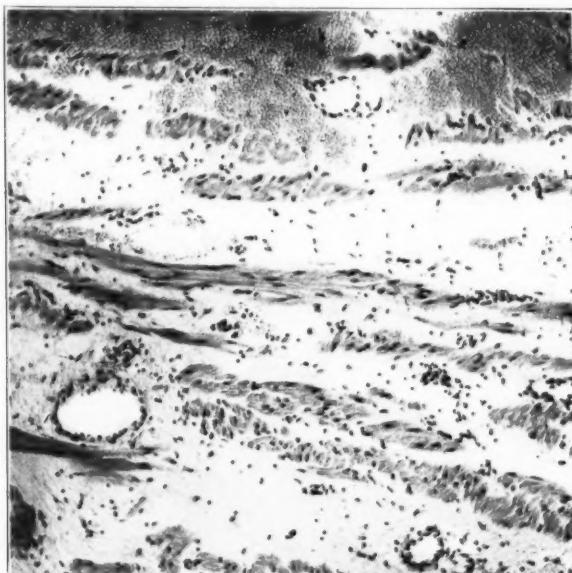


Fig. 7.—Wall of human uterus, removed for premature separation, showing disassociation of muscle by edema and hemorrhage. Note clasmacytotes in the edematous area.

observed on the surface of human uteri in cases of premature separation of the placenta. (Fig. 5.) After hardening in 10 per cent formalin, the affected portion of the uterine horn was opened and a noteworthy phenomenon observed in its mucosa, namely, a conspicuous hemorrhage extending along the course of blood vessels corresponding to the purplish spots mentioned above. The placenta did not show any sign of separation. Upon histologic examination, the occurrence of a marked edema, which spread apart the muscle bundles, was a striking feature, resembling the conditions encountered in the human uteri. (Figs. 6 and 7.) Furthermore, the occurrence of clasmacytotes in the edematous areas—quite similar to the observations of Williams on uteri removed for premature separation of the placenta—strengthened our conception that both conditions are closely allied. (Fig. 6-A.)

A few words concerning the findings in the uterine mucosa in the areas in which hemorrhage had occurred. The essential finding in

such areas is that the uterine glands adjacent to the placenta are filled with fresh blood, which in places has lifted up the covering layer. Under higher magnification, it was clear that red blood cells had made their way into the lumen from dilated capillaries beneath the glands by following the interstices between adjacent epithelium cells. In conclusion, it may be added that in some of our experiments, the abdominal cavity contained a variable amount of free fluid, which was very abundant in a few instances. This point appears to be of special interest, since our observations and the reports of others dealing with the findings upon opening the abdomen in cases of premature separation in women almost invariably mention the presence of a certain amount of free yellowish or bloody fluid.

Furthermore, we may mention the occurrence of petechial hemorrhages in various organs of the experimental animals, especially in the spleen and the pancreas. Our special interest, however, was aroused by the changes encountered in the liver and the kidney. While these lesions will be described in some detail in a later section of this paper, it may suffice to mention here that in carnivora the occurrence of peripheral liver necroses of the anemic and hemorrhagic type, associated with thrombi in the vessels, constituted a striking feature. Degenerative changes in the epithelium of the convoluted tubules of the kidney were an additional striking phenomenon.

Summing up the results obtained, we may say that the essential features of the clinical picture of premature separation of the normally implanted placenta, as it occurs in women, have been reproduced in pregnant animals by the intravenous administration of histamine: namely, the separation itself, marked shock, engorgement of the vessels of the uterus and broad ligament, uterine spasm, hemorrhages in various organs, and histologically edema of the uterine wall and degenerative changes in the liver and kidney. At the same time, it is clearly recognized on our part that in spite of so close a resemblance in the syndromes, our experiments cannot be regarded as conclusive until the presence of histamine or histamine-like substances has been actually demonstrated in the blood of patients presenting premature separation. As a matter of fact—as far as such evidence can actually be adduced—this must be regarded as the ultimate test of the validity of the conclusion that premature separation of the placenta is a histamine effect.

The recent work on the pathology of premature separation, in which the names of Couvelaire and Williams figure prominently, discusses at length the clinical phenomena of the condition and the anatomic lesions, with special reference to the hemorrhages in the uterine wall and the details of the vessels. Considering the etiology, Williams has disposed of various factors whose causative significance

had previously been emphasized in the considerable literature upon the subject, particularly the presence of inflammatory conditions in the decidua basalis and trauma, and he states: "As yet, we are entirely ignorant of the ultimate cause of the accident and can do little but speculate concerning it." Upon studying the older literature upon the subject, it was interesting to me that the view that the action of some chemical substance was responsible for the damage to the vessels, and was therefore the primary cause of the condition, had already been surmised by Spiegelberg, who stressed the significance of certain alterations in the vessel walls resulting from an unknown anomaly of the blood. The point to be emphasized here is that the preponderance of evidence now tends to show that premature separation of the placenta, from being a purely local condition, has become one which involves the whole organism, and a number of observations made in recent years, which indicate some association between accidental hemorrhage and eclamptic conditions, afford confirmatory evidence of the truth of such reasoning. Consequently, in the last decade the significance of a toxemia as an etiologic factor in at least the majority of the serious cases has been urged. "The chief argument in favor of this theory is based upon the sudden onset of the accident, its occasional occurrence in toxemic or eclamptic women, the occasional demonstration of degenerative lesions in the kidney or liver, but particularly upon the presence of albuminuria, in a large proportion of the patients" (Williams). At this juncture it may be noted that during the last few years a number of additional cases have been reported in which premature separation has occurred in patients who were under observation on account of pre-eclamptic toxemia or eclampsia. The opinion, therefore, that both of the conditions are closely allied, or perhaps identical, is gaining ground, so that it may be permissible to group such cases under the heading *Hepatotoxicemia* or *Pre-eclampsia*. In this connection, the reader is referred to the articles by Portes, Le Lorier, Holmes, Scott, Gordon-Ley, Phaneuf, Heynemann, Fordyce, and Klaften. And our observations as to the experimental reproduction of characteristic changes in the liver and kidney accord well with such a view, but it is only fair to state that Williams does not feel that the evidence thus far adduced in the literature should be regarded as conclusive.

A satisfactory explanation of the mechanism which in all probability operates in the premature separation of the human placenta, seems to be afforded by the phenomena observed, which indicate that a sudden distention of the maternal blood spaces in the placental district accounts for the production of the accident under experimental conditions. We must recall that in our experiments hemorrhages occur in various regions as the result of special local peculiarities, par-

icularly when the dilated vessels were supported by rather delicate tissues. The observation in premature separation of the human placenta that the decidual vessels have become dilated into enormous thin-walled sinuses, linked up with the statement that hemorrhage into the depths of the decidua appears to be the immediate factor in bringing about the detachment of the placenta, gives a clear hint as to the nature of the process. As Williams has pointed out, "It is only necessary for minute hemorrhages in the decidua basalis to coalesce in order to inaugurate the process which once begun will continue and be stimulated by the enclosed collection of blood acting as a foreign body." Frankl and Hiess, who hold that even the normal detachment of the human placenta is preceded by a distention ad maximum of decidual vessels and subsequent rupture, consider premature separation of the placenta as a pathologic condition which has its prototype in physiology, the difference lying solely in the fact that, in the latter case, the overfilling of the vessels takes place while the child is still within the uterine cavity.

Since from the above experiments it is clearly seen that there exists a suggestive analogy between histamine intoxication and the clinical phenomena of premature separation of the human placenta, a number of points of view from the therapeutic standpoint must be considered. In discussing shock in both conditions—premature separation and acute histamine intoxication—I point out that an overfilling of the vessels in the splanchnic area, associated with an increased permeability of the vessels for the escape of fluid, accounts for this accident. The very point that the volume of blood in actually effective circulation during shock is greatly reduced by these factors has been fully recognized only in recent years. This fact, however, has an important bearing upon the problem of early treatment which may be outlined here in skeleton form. The really vital matter in the treatment of shock consists in direct methods for restoring the blood volume and in the application of heat. The urgent immediate need of vascular fluid—according to the statements of the Medical Research Committee on Shock in London (1919), is effectively met by the transfusion of a sufficient quantity of blood or 5 to 6 per cent gum-saline solution. In order to obtain a more immediate response, transfusion of blood is preferable. Saline solution can be forced by rectum by the drip method. Accordingly, *transfusion* plays a prominent part in the treatment of premature separation of the normally implanted placenta, and I would suggest the delay of operative interference in severe cases until the effect of immediate transfusion has become well marked.

Before leaving this subject it may be well to discuss another point of clinical significance. The experimental work of Bayliss, Dale, and others indicates that ether, by virtue of its toxic action on the endothelium, greatly enhances the effect of histamine: an observation

which accords remarkably with the clinical experience that the administration of ether is most dangerous in persons who are threatened with shock and that its poisonous effect persists for some time after the anesthesia is discontinued. Furthermore, it must be borne in mind that any existing toxemia is greatly intensified by the administration of anesthetics. Consequently, if our conception of the ultimate cause of the *premature separation of the placenta* and of the *clamptic condition* be correct, it would seem fair to conclude that *local anesthesia*—combined with nitrous oxide and the free use of *oxygen* should be the rational mode of procedure in patients presenting these accidents.

## II

Since the present studies are chiefly concerned with the poisonous effect of histamine, particularly in regard to the vascular system and the parenchymatous organs, a few remarks concerning the nature and the properties of this substance may not be out of place. The numerous researches and discussions on the subject in general testify to the live interest and vigorous development in this field, and I would especially refer to the brilliant work of Abel, Dale and coworkers. Histamine is derived by removal of the carboxyl group as  $\text{CO}_2$  from histidine, one of the most important building-stones of the protein-molecule, and is known to be formed as the result of bacterial activity in the intestinal canal. Its precursor originates as a product of the intermediate protein metabolism in animal tissues. A very slight modification of the protein molecule is sometimes sufficient to change it to a poison having the characteristics of the *histamine group*, which consists of a number of protein derivatives of unknown structure. "And the ease with which *histamine-like* substances are split off from cells of all kinds, inevitably suggests the preexistence of a grouping which can readily be detached by any influence which injures the vitality of the cells, and then is capable of producing the series of associated physiologic effects characteristic of histamine. The fact that extracts of so many organs and tissues contain substances exhibiting this type of activity, must have some physiologic significance. Evidence has been presented which reinforces the suggestion that action of the histamine type is one of genuine physiologic importance, in providing at least in many species, one side of the balanced chemical control of capillary tone, of which the other is provided chiefly by the natural secretion of adrenalin. The action of histamine on the blood vessels involves a dual mechanism, an increase in the tone of the arterial plain muscle and a relaxation of the tone of the capillaries" (Dale and coworkers).

Injected intravenously, histamine soon causes the arterial blood pressure to fall to the shock level, and the recognized failing output of the heart is considered as the result of two factors. In the first

place, much of the blood is withdrawn from the circulation by stagnation in dilated vessels (capillaries and venules) particularly in the splanchnic area; and in the second place histamine abolishes the tone of capillaries at the same time that it increases the permeability of their walls and thus permits the plasma to leak out. The only point needing additional emphasis concerning the action of histamine upon the vascular system, is that the evidence available goes to show that in the living animal larger doses of histamine are liable to produce vasoconstriction. (Dale, Kellaway, Ebbeeke, McDowall, Rothlin.) And it should be added that histamine is known to act as a lymphagogue par excellence, and, in addition, to increase the excitability of the vegetative nervous system. Histamine is also a powerful agglutinator for human erythrocytes (Hanzlik). Its relation to the products of certain ductless glands (pituitrin, adrenalin, insulin) will be referred to in a later section of this paper.

After this digression, we return to our experiments and shall now discuss a series of further observations which were made incidentally upon the liver and kidneys of pregnant dogs which were subjected to repeated injections of small amounts of histamine for a considerable period of time. As we shall see later, these experiments were performed with the direct object of determining whether previous treatment with repeated doses of histamine does or does not affect the susceptibility of the arterial system toward adrenalin.

The following protocol illustrates the mode of procedure: Pregnant dog at term, weight 13 kg., received daily during the course of one week an intravenous injection of 0.5 mg histamine. Following the ninth injection, the animal gave birth to five well-developed living puppies. The next day, under ether anesthesia, blood pressure tracings were taken, and at the end of the experiment the animal was sacrificed and the abdominal organs immediately removed. The liver was normal in size but somewhat flabby and presented a strikingly mottled appearance and a yellowish color, which on section was found to extend throughout the organ. Fig. 8 represents the microscopic picture of the liver, and shows a widespread degeneration of the center of the lobuli. Closer study shows great variation in the extent of damage. A few cells appear to have undergone complete destruction, while in the vast majority the outlines of the nuclei, while still visible, are frequently pushed to the periphery of the cell. The cytoplasm appears either highly vacuolated or altogether transparent. Since the cells at the periphery of the lobules show but slight granular degeneration or present a cloudy appearance, the contrast between the clear central area and the darker peripheral zone is very striking. Moreover, frozen sections stained with selenite III reveal an intense fatty infiltration particularly in the central portion of the lobules; while faint, irregularly shaped spots in the center mark little necrotic areas. Glycogen has disappeared throughout, except for small remnants at the periphery of the lobules. Consequently the changes in the liver closely resemble those occurring in fatal cases of pernicious vomiting, as described by Williams, Hofbauer and others. A further similarity between such findings and those produced experimentally in our investigations is likewise presented by the kidney. As was pointed out in my monograph on the *Toxicoses of Pregnancy*, it is the epithelium of the convoluted tubules which exhibits marked

degenerative changes and stands out conspicuously if specifically stained for fat. Fig. 9 represents a section of kidney from one of our experiments; it clearly shows the changes. An additional link in the chain of evidence showing how closely the microscopic features in both conditions simulate each other, is afforded by the dilatation of the small and smallest vessels in the liver, as well as in the kidney.

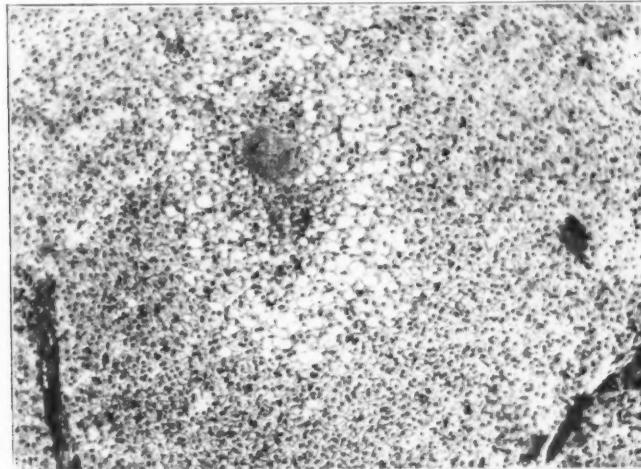


Fig. 8.—Liver of dog after administration of histamine for ten days, showing fatty infiltration of liver lobules.

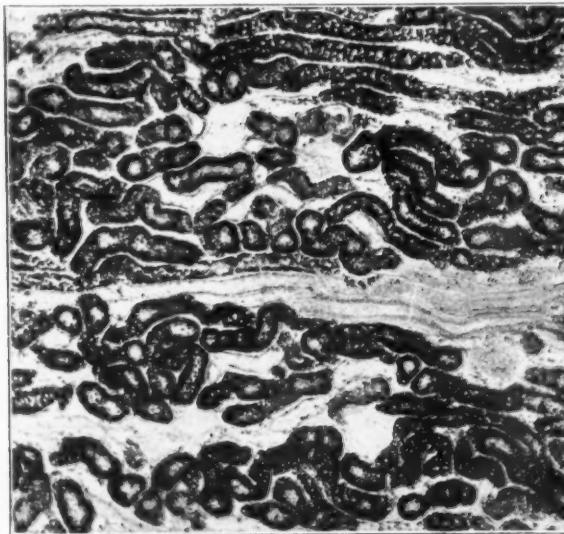


Fig. 9.—Kidney of same dog, stained with sudsan III, showing fatty degeneration of convoluted tubules.

Whatever may be the final interpretation of the facts here recorded, a number of further data obtained in the investigation of histamine intoxication renders certain clinical aspects of the condition under

consideration more intelligible. When histamine is subcutaneously injected into carnivora a marked salivation soon sets in, and is accompanied by an increase of the secretion of gastric juice. Furthermore, experimental data are on record which show that histamine may act as an emetic, the stomach showing increased hypertonic contracture. To forestall objection, however, it should be stated frankly that the assumption that the clinical and the experimental phenomena are identical, should at present be regarded merely as a theoretical possibility.

Our special interest was focused upon the condition of the liver for the reason that many of the recent articles dealing with hyperemesis insist that glycogen deficiency of the liver dominates the clinical picture, and is even regarded as the etiologic factor concerned in the production of the condition (Harding, Titus, Thalhimer, Frey). It may be of interest to note that in my monograph on the subject, I was the first to point out the significance of glycogen deficiency in the liver and placenta, and that I suggested a functional test of the liver by using levulose.

Before leaving this subject, it may be well to state that Dr. Geiling and I are now conducting a series of experiments with the object of ascertaining whether the intravenous administration of insulin or glucose—when given for a period of two weeks simultaneously with histamine in the same doses as in the above experiments—will prevent the occurrence of fatty infiltration of liver and kidney. The immediate impulse for such experiments was furnished by the statement of Macleod and Noble that glycogenolysis due to adrenalin can be inhibited by insulin. While the results of our experiments are to be published in some detail on another occasion, it is interesting to note that microscopic examination of the organs shows that quite normal conditions of both liver and kidney are maintained when histamine and insulin are given simultaneously or in short intervals between each other. Glucose prevents to some extent the occurrence of necrotic processes in the liver. Thus, it appears that a hitherto unknown principle of insulin is in operation in this field of the economy of the organism. In the present preliminary report, however, we shall refrain from discussing the clinical bearing of these observations.

### III

In the first section of this paper, when referring to changes encountered in the liver and the kidney of carnivora in acute histamine intoxication, it was stated that information was available in support of the view that premature separation of the placenta is frequently associated with pre-eclampsia. The point to be emphasized here is that changes in the liver identical with those described as characteristic of eclampsia have not only been reproduced in response to his-

tamine, but also that the individual specimens show a variety of certain changes as is the case in eclamptic conditions. The noteworthy phenomenon is the occurrence of peripheral necrotic foci of both the anemic and of the hemorrhagic type. No explanation can be offered for the marked difference in the sensitiveness of various animals toward histamine. Nor is it clear why the response to the drug led to the anemic type of necrosis in one instance and the hemorrhagic in another.

*p.s.p.*

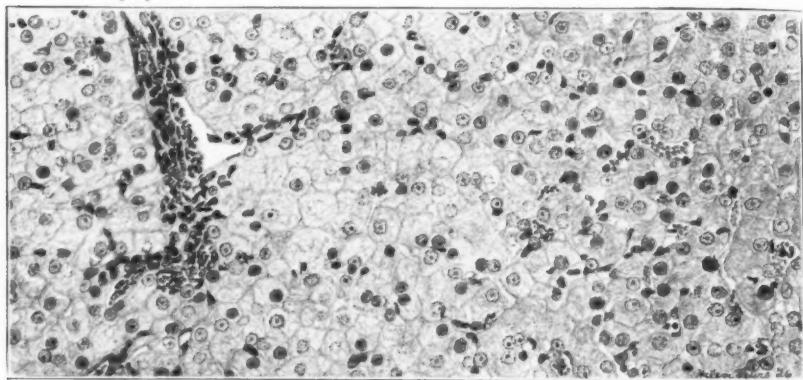


Fig. 10.—Liver of pregnant cat after acute histamine poisoning, showing necrosis in peripheral portion of lobule. *p.s.p.*, portal space (Glisson's capsule).

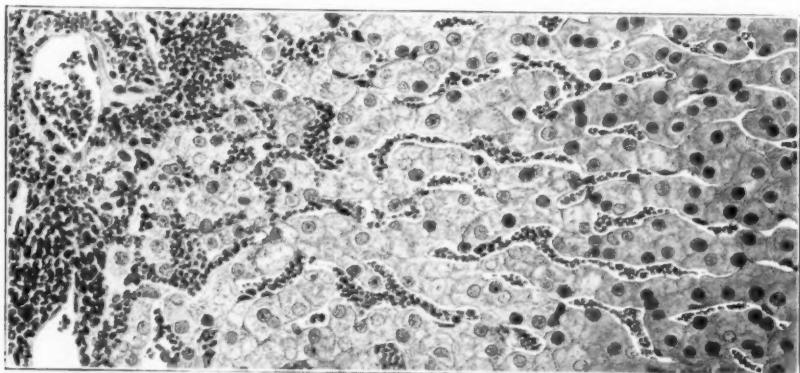


Fig. 11.—Liver of pregnant dog after acute histamine poisoning, showing hemorrhage into periportal space and hemorrhage and necrosis in peripheral portion of lobule. Note dilatation of capillaries.

The changes in the liver are well illustrated in Fig. 10. This represents a section of the liver from the experiment described above (chloralose anesthesia) and shows a marked difference between the periphery and the center of the lobule. Even under low magnification the periphery is in general lighter and the structure of its tissue rather indistinct. Under higher magnification, the clear appearance of the zone is seen to be due to the fact that the cytoplasm has lost its granular structure as the result of a total vacuolization or a cloudy swelling of the cells, which is accompanied by an increase in their size. In some places, however, the nuclei of the liver

cells are invisible, while the boundaries of adjacent cells can hardly be differentiated. Moreover, a characteristic feature consists in a distinct increase in size of the Kupffer cells. Frozen sections stained with selenite III fail to reveal the presence of any noticeable quantity of fat within the degenerated areas. The conspicuous feature of Fig. 11, which represents a section of a liver from an experiment without anesthesia upon a pregnant dog practically at term, consists in extensive hemorrhages in Glisson's capsule. While the small arteries are completely constricted, the branches of the portal vein are dilated and about their walls hemorrhage has occurred, which in places extends into the periphery of the lobules. In such areas the liver cells have undergone necrosis, probably as the result of pressure exerted by the effused blood. Fig. 12 shows the topography of hemorrhagic lesions. In some places the development of thrombi can be observed—which are sometimes of the hyaline type, while others consist of clustered erythrocytes with platelets. Sections stained by the methods of Mallory, Koekel, van Gieson, now and then show the presence of

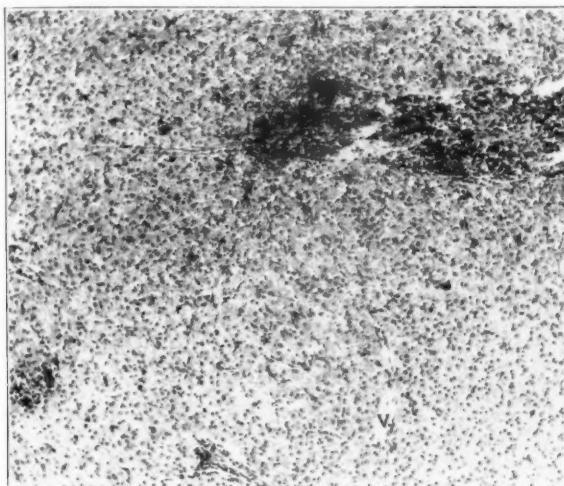


Fig. 12.—Photomicrograph of liver of Fig. 11, showing topography of hemorrhagic lesions. V., central vein.

fibrin in the degenerated areas. Another striking feature consists in a marked distention of the lymphatics in the connective tissue of Glisson's capsule similar to the observations in eclamptics.

The parallel between the lesions which we have described and those noted in actual eclamptic livers becomes even more suggestive when it is recalled that a definite precipitation of bile pigment can be observed within the liver cells in a number of instances, while in other places there is a marked dilatation of bile capillaries. In my monograph on the *Toxicoses of Pregnancy* I explained that we have to deal in eclampsia with a stagnation of the bile, and Fahr has recently insisted that bile stasis constitutes an essential feature of the eclamptic liver. This statement receives additional support from the observations of Gegenbach, Süssstrunk and Eufinger that the quantity of bile pigment in the blood of eclamptic patients is definitely increased.

The essential changes in the kidney consist of degenerative lesions of the epithelium of the convoluted tubules, which in some places is deprived of nuclei, and the occurrence of delicate fat droplets in the endothelium of the malpighian bodies. The capillary vessels are distended. Hyalin thrombi appear in various areas. Coagulated masses are to be found within the lumen of the tubuli, and in a few instances a number of erythrocytes are present (Fig. 13).

In seeking an explanation for the changes in the liver in acute histamine intoxication, a hint is possibly provided by the belief of B. Fischer that vacuolization of the liver cells should be regarded as a symptom of water-intoxication, which makes its appearance particu-

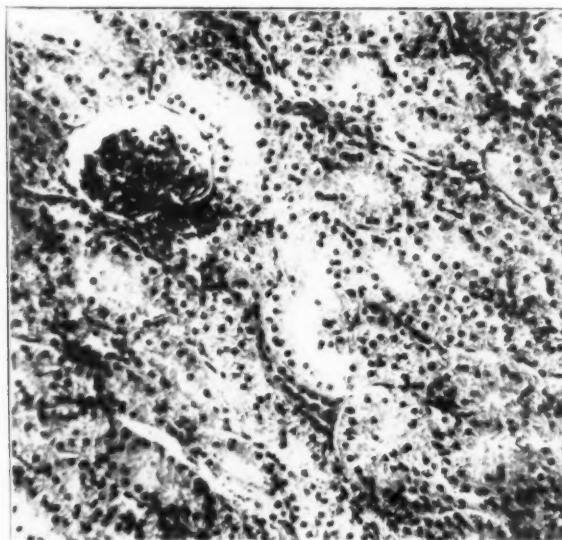


Fig. 13.—Photomicrograph of kidney of dog, whose liver is shown in Fig. 11, showing degenerative and necrotic changes in convoluted tubules.

larly in the periphery of the lobules, shortly after the ligation of the ductus choledochus.

Without considering all of the implications of our experiments, one point may be touched upon which is especially applicable to clinical conditions, and that is that we have to deal with a stasis of the bile. When we come to discuss the actual mechanism by which it is brought about, we should recall the fact that histamine, which is a smooth muscle stimulant in certain circumstances, causes contraction of the Oddi sphincter—a system of smooth muscle fibers at the entrance of the common duct into the duodenum. In this connection brief reference might be made to the observations of Westphal, who showed that in examining pregnant women by the duodenal tube, an increased irritability of the Oddi sphincter may be noted as a response to the

administration of pilocarpine. It would seem to be a matter of indifference whether the resistance noticed to the flow of bile into the duodenum is induced by the tonus of the muscle wall of the duodenum, or by the tonus of the sphincter of Oddi itself; but the practical aspect of the matter is that such observations may afford a plausible interpretation for the production of the epigastric pains, which are justly regarded as an important premonitory symptom in eelamptic conditions.

In our studies considerable attention has been given to another problem, namely, the cause of the elevation of blood pressure which occurs in pre-eelamptic and eelamptic conditions; and the possibility of correlating it to our new trend of argument. At first glance, the very fact that histamine is known to be attended by a marked fall in blood pressure seemed incompatible with the conception of an inverse reaction. The more, however, we began to study the subject, the more we met with authoritative statements that histamine, although a capillary dilator and capable of bringing about shock if absorbed in large quantities, may in certain circumstances evoke constriction of arterioles. First of all, as shown by Dale, histamine has a definite constrictor action on smooth muscle structures, and reference has already been made to a number of articles which stress its vasoconstrictor effect upon the systemic arterioles. Furthermore, the experimental work of Dale and Richards, Kellaway and Cowell, Backman and Hultgren, has disclosed the interesting fact that in the normal animal even a small dose of histamine accelerates the secretion of adrenalin. Moreover, Dale considers that a normal function of adrenalin is the maintenance of capillary tone against the depressor action of the products of cellular injury or metabolism. A similar view, as to the antagonistic effect of histamine and adrenalin on the capillaries, has been brought forward by Ebbeeke, Krogh and others, who hold that pituitrin is likewise concerned in the maintenance of a normal equilibrium. Moreover, the experiments of Blau and Haneher tend to show that the absorption of histamine is correlated with increased influx into the cerebrospinal fluid of pituitrin. Furthermore, Kellaway's experiments go to show that histamine causes an increased output of adrenalin, and that adrenal insufficiency in turn results in hypersensitivity to histamine, and a most recent paper by Burn and Dale emphasizes the point that there is sufficient evidence that a secondary *pressor effect* of histamine is due to accelerated output of adrenalin.

Our investigations have primarily aimed to obtain orientation as to whether an altered response to adrenalin can be detected in pregnant carnivora which had previously been subjected to the administration of small doses of histamine for a week or more, particularly in view of the claim of Hülse that peptones exert such an effect by rendering the

arterial system more susceptible to adrenalin, and that similar phenomena may be observed upon the application of eclamptic serum to isolated arteries. In our experiments, the pregnant animal (dog or cat), was given intravenously 0.5 e.e. of a 1:1,000 solution of histamine daily for seven to ten days. Then under ether or urethane anesthesia the carotid was dissected out, care being taken not to injure the vagi, and the cannula inserted into it by which the blood pressure could be recorded. After a suitable level had been attained, adrenalin (1 e.e. of 1:200,000 down to a 1,000,000 solution) was injected into a femoral vein. Histamine was then injected and another reading made to ascertain the effect of a similar dose of adrenalin. While the tracing shows that the first injection of adrenalin gave an inverse reaction (depressor effect), a second dose of adrenalin produced the usual and characteristic elevation (pressor effect), after the animal had recovered from the fall in pressure produced by histamine. Again there are some other observations on low blood pressure produced by histamine and the effect of adrenalin which raises the blood pressure, often for a longer time than would be expected from the dose given. The results obtained, however, are advanced with reservations, and only as subsidiary evidence that a change had occurred in the tone of the arteries. At the same time, our experiment offers a certain analogy to the statement made by Louros that adrenalin injected into eclamptic patients produces an inverse effect. These observations made clear the importance of the composition of the tissue fluids in determining the response to a well-known pressor substance.

A comment may be interjected here. It has been shown by Kylin and subsequently by various writers (Janssen, Kaufmann, etc.) that in essential hypertension the response to adrenalin is manifested by a primary fall of blood pressure and that the phenomenon is significantly dependent upon the electrolytes. That is, any change in the K/Ca ratio, which is normally 1.0 to 2.15, in favor of the preponderance of *K*, is accompanied by a reverse (*vagotonic*) type of adrenalin response. This observation is of interest from the fact that a similar alteration in the ratio of the electrolytes occurs in pre-eclamptic and eclamptic patients. Furthermore, Zondek claims that under experimental conditions the histamine effect is equivalent to a decrease of the calcium content in the tissues and can be counterbalanced by either adrenalin or calcium.

In reviewing the recent literature dealing with the problem of hypertension one can hardly escape the impression that its etiology is still an unsolved problem. There are, however, certain recent advances which have resulted from the active study in this field which deserve special emphasis: first, the recognition that the excess of pressure is conditioned mainly by functional variations in the tonus

of the arteries and arterioles, and that the general arterial constriction is due to an altered condition of the vasomotor centers in the midbrain (hypothalamic region) and in the medulla. Finally, as has already been mentioned, electrolytes may play a material part in the production of such conditions. The latter point has been especially elaborated by Kraus and his coworkers, who give their conclusions as follows: "There is an intimate relationship between the activity of the vegetative nervous system, the ductless glands and the electrolytes. The products of the ductless glands exert a definite influence upon the vegetative system, while the latter ultimately controls the action of the hormones. The distribution in the cells of the electrolytes being essentially controlled by both the hormones and the vegetative nervous system determines in turn the effect of the hormones. Endogenous poisons may act by changing the reciprocal proportion of electrolytes (K, Ca). The whole system of electrolytes in the body represents an entity, and their demonstrable changes in the blood are indicative merely of a derangement having taken place, which as a consequence may give rise to a variety of symptoms, for example, vasoconstriction."

While I feel that our conception as to the actual cause of the elevation of blood pressure, in both its systolic and diastolic phases, as far as the toxemias of pregnancy are concerned still remains inaccurate, yet considerable evidence as to the correctness of the view that it is due to a toxic alteration of the capillaries of the brain and vasomotor center has lately been brought forward by E. H. Starling. For this reason his statements will be quoted verbatim: "The arterial blood pressure is the resultant of two factors—namely the output of the heart and the peripheral resistance. The peripheral resistance is maintained by the tonic contraction of the arterioles, especially of the splanchnic area and is thus under the constant control of the vasomotor center working through the sympathetic system. Our recent experiments show that the vasomotor center is acutely sensitive to the slightest alteration in the blood flow through it. The smallest increase in this flow causes vasodilatation and therefore a fall of blood pressure, while the slightest decrease brings about general vasoconstriction and a rise of blood pressure, and these effects are permanent—that is, last as long as the alteration which is effected in the vasomotor center. All the mechanisms for the regulation of the activities of the heart and arteries are directed toward the maintenance of a blood flow through the capillaries in accordance with the needs of the tissues they supply. First among these needs are those of the vasomotor center and brain. There is evidence that in many parts of the body—perhaps in all—the capillaries are endowed with contractility, and this properly must be a considerable

factor in regulating the irrigation of the tissues according to their activities. Any such contraction of the capillaries to the vasomotor center would evoke an immediate response and rise of arterial pressure lasting as long as the contraction of the capillaries. But we know that the capillaries are susceptible to other chemical influences which alter their permeability—that is, the amount of blood fluid which filters through their walls. A familiar example of such a change is the wheals produced in the skin as a result of the injection of certain animal poisons or by the local injection of substances such as *histamine*. Any similar change in the capillaries to the brain would be fraught with evil results for the circulation through them; for it must be remembered that these capillaries run in a pericapillary lymphatic; increased exudation would cause a rise of pressure in the lymphatic and a corresponding narrowing of the lumen of the capillaries. *I would suggest that such a condition of altered capillary wall is responsible for the high arterial pressure which is the invariable concomitant of certain toxic conditions such as uremia and the toxemia of pregnancy.* In both of these, the high pressure I have ascribed to interference with the capillary circulation to the vasomotor center is accompanied by well marked signs of deficient circulation through other parts of the brain, such as headache, amaurosis, temporary loss of speech, various paralyses, and convulsions; and we know that in the toxemia of pregnancy at any rate, all these symptoms may subside with the termination of the pregnancy."

Roberts likewise emphasizes the fact that a slight diminution in the blood supply stimulates the vasomotor center and furthermore points out that laetic acid—the presence of which in the cerebrospinal fluid of eclamptic patients has been demonstrated by Füth and Loekemann in 1906—excites the vasomotor center to further activity. For more detailed information concerning the effect of a curtailment in the blood supply as a stimulant for the hypothalamic vasomotor center and for an adjacent center concerned with the discharge of epinephrin from the adrenals, the reader is referred to articles by Dresel, Houssay and Molinelli, Tournade and Chabrol.

With reference to the chemical findings in eclampsia, it should be mentioned that the writer has identified amino acids, laetic acid and purin-bodies in the liver (Monograph on *Toxicoses of Pregnancy*). Hence, the process has been designated by him as *partial autolysis of the liver*. It is the occurrence of autolytic processes in the liver which induced him to stress in that monograph the importance of discarding chloroform in operations upon eclamptics—in accord with the rules laid down by clinicians and pharmacologists that both chloroform and ether are contraindicated as anesthetics in any case of tissue damage in the liver (Osborne). In addition, the investigations of Stander and Radelet in this Clinic, which will soon be published, show that hyper-

glycemia, and an increase in lactic acid, uric acid and the inorganic phosphates in the blood constitute the essential changes in the eclamptic condition. Furthermore, similar changes have recently been reported in canine anaphylaxis and in acute histamine intoxication, by Chambers and Thompson. The exact significance of such alterations is still *sub judice*, but there is considerable evidence that they may be intimately connected with tissue damage in the liver. Should these observations be confirmed by further investigation, they would lend support to the view that the blood changes in the several conditions run parallel to the alterations in liver function.

Since the histamine effect and the anaphylactic phenomena so closely resemble one another in their clinical behavior as to be somewhat difficult of differentiation, and since certain investigators have attempted to explain eclampsia as an anaphylactic reaction, a few words concerning the problem may not be out of place. My experimental researches published in 1909 and 1910 indicated that the anaphylactic theory of the toxemias of pregnancy was not applicable, particularly because the injection of fetal serum failed to evoke anaphylactic reactions in pregnant and puerperal women. My conclusions were confirmed by a number of further investigations (Johnstone, Eisenreich, Murray, E. Zweifel and others), and it is now generally believed that this theory can no longer be maintained. On the other hand, it must be admitted that some color is lent to it by the fact that the histamine effect and the anaphylactic reaction, although not identical, do present certain striking similarities (Dale).

An interesting observation strongly indicating the occurrence of changes in the cell activities in eclamptic condition, has been published recently by Benda, who showed by means of the uranium and bromide technic, as well as by the hemolysin reaction, that the permeability of the meninges and of the choroid plexus is greatly increased in eclampsia. If these observations are confirmed, they would appear to indicate that the metabolism of the brain and the conditions of intracranial pressure might be materially interfered with and the occurrence of convulsions be favored. This conception receives additional support from the studies of Sioli on the small vessels in the brain of eclamptic patients. He found a fatty infiltration of the endothelial cells associated with definite swelling and proliferation of their nuclei. In this connection, it is interesting that in other organs—particularly in the liver, spleen, kidney and lungs—the occurrence of degenerative changes, or an actual swelling of the endothelial cells has of late been demonstrated independently by Fahr and Domagk; these afford morphologic evidence of the action of a special endothelial toxin in eclamptic conditions.

That a leakage of plasma from the blood stream into the tissues actually takes place in eclampsia is indicated by the observations of

Zangemeister that the red blood count may increase to as high as nine millions, provided that the activity of the kidney has not been materially impaired. Furthermore, it must not be forgotten that histamine and pituitrin increase the osmotic pressure of the proteins, and by so doing, enhance the water-binding power of the tissue and promote the development of edema as shown by Ellinger, Molitor and Pick. And both of these factors, the osmotic pressure and particularly the degree of permeability of the endothelium, are materially involved in the mechanism of water-exchange between tissues and the blood stream.

In summing up, it is apparent that the supposed mechanism involved in the production of the phenomena observed in our experiments rests upon the action of a special endothelial toxin, which renders the capillaries more permeable to the escape of fluid. It would therefore appear that the histamine effect in all probability rests upon a physicochemical basis. At the same time this toxic substance is seen to act as a hemorrhagin and by changing the actual constitution of the blood to favor the agglutination of its red cells. In addition to the thrombosis, which may initiate the periportal necrosis of the liver, must be added the stagnation of the bile caused by the spasm of smooth muscular structures at the orifice of the common duct—the response to histamine.

In the light of the pathogenesis of eclampsia as set forth here, due consideration should be given to the following points of view in the treatment of this condition. In the first place, the occurrence of autolytic processes in the liver in eclamptic patients compels us to focus our attention upon those factors which are known either to retard or to hasten this process. In this respect, a diminution in oxygen supply is recognized as having an injurious effect upon living cells, particularly those of the liver and to add its ill effect to the deleterious action of substances like histamine, chloroform, ether. On the other hand, it is important to remember that an abundant supply of oxygen to the tissues in the first stage of autolysis decidedly retards the process, greatly lessens the after effects and aids recovery (Laqueur). Furthermore, want of oxygen calls forth an increased state of activity of the vasomotor center, resulting in a constriction of the peripheral arterioles (Starling), and in addition, excites the flow of adrenalin into the blood current which assists in the rise of blood pressure (Bayliss). Oxygen starvation also rapidly increases the permeability of the capillary wall (Bayliss) and promotes the elaboration of cerebrospinal fluid (Dixon). Finally, since the nerve cell shows a great dependence upon an abundant supply of oxygen, the damage of the nerve centers due to oxygen deficiency may impair the vital functions of the body. In addition, the administration of oxygen often acts as a primary cardiac stimulant. The advantages of a liberal and continu-

ous administration of oxygen in eclamptic conditions, based both upon laboratory findings and clinical observations, have been emphasized by the writer in 1912 in his monograph on this subject. Since the physiologic principles involved in this treatment are now better understood and my experience with this method has advanced, I am inclined to advocate the routine early administration of oxygen in severe cases of eclampsia as a valuable element in the program of the treatment—a safeguard against irreparable damage to vital organs. The length of time during which the inhalation should be continued, as a matter of fact, varies with the gravity of symptoms. The supply of oxygen is in some cases required for days. In other words, the liberal administration of oxygen is to be maintained until cyanosis practically disappears.

The importance of the administration of glucose in eclamptic conditions, as advised by Titus and others, is evident when we realize first, that glycogen disappears from the periphery of the liver lobules in eclampsia; and secondly, the changes observed in the liver during starvation, when superimposed upon eclampsia tend to increase the existing acidosis. Furthermore, the above-mentioned observation, that in experimental conditions the administration of glucose protects the liver cells against chemical damages, furnishes an additional basis for the valuable aid rendered to eclamptic patients by the administration of glucose. The therapeutic importance of glucose as a cardiotonic has been recognized in recent years.

#### IV

On several occasions I have intimated that a certain amount of conservatism is necessary in transferring conclusions from experimental results in animals to morbid processes in man. Consequently, it is perfectly reasonable to entertain doubt of the significance of histamine as the etiologic factor in the production of the toxemias as long as actual chemical demonstration of its presence in the circulatory fluid has not been adduced. The criticism, however, loses a part of its force when we remember that the normal activity of any hormone or other potent metabolic product is probably the result of the steady production of such minute amounts of the principle that they are difficult to detect even by the most delicate chemical reactions. In this connection it should be remembered that according to the experience of the pharmacologists the acute toxic dose of histamine is smaller than that of any amine which has been studied up to this time. Furthermore, when the substance is given slowly, far more than the acute lethal dose can be administered, since in such circumstances its toxic influence is decreased by deamidation and oxidation in the body of the animal. And histamine is readily taken out of the blood by the tissues. Consequently, the actual demonstration of the presence of

histamine in the blood would indicate a very acute poisoning, so that when the poisoning is somewhat prolonged, it could scarcely be expected that the presence of the substance could be demonstrated at all (Loeffler). Furthermore, it must again be remembered that pure histamine and the various substances in the *histamine group* have a similar biologic effect upon the vascular system.

As a test for the presence of histamine in the blood, a color reaction with p-phenyldiazonium sulphonate has been suggested by Hanke and Koessler, but its value has not been proved. Nor are the widely used biologic tests established upon a firm foundation. These are based upon the ability of histamine to produce contractions of the uterus and the small intestine of the virgin guinea pig, on one hand, and of the vessels of the perfused rabbit's ear, on the other. Such experiments caused Hüssy and his coworkers to claim several years ago that eclampsia, pre-eclamptic toxemia, and severe cases of hyperemesis were due to the presence of *biogenetic amines* in the blood; whereas in the serum of normal pregnant women they were unable to demonstrate the presence of any vasocostrictor substance.

At the same time it might be mentioned that investigations which are being conducted in this department by Dr. K. C. Sun show, in certain cases at least, that the blood freshly drawn from pre-eclamptic and eclamptic patients before any treatment is instituted, does contain some substance or substances which increase the tonus and amplitude of the contractions of the uterus of the virgin guinea pig suspended in Tyrode's solution. Such an observation is the more remarkable, as it is conceivable that the presence of lactic acid, as demonstrated by Zweifel in the blood of eclamptic patients in 1906, might so alter the hydrogen-ion concentration of the blood as to produce a definitely inhibitory effect upon such contractions. The similarity of such a kymograph tracing and a tracing showing the characteristic histamine effect is demonstrated by Figs. 14 and 15.

I will now give my views as to the possible development of histamine in the pregnant organism, as well as to the biologic purpose it may serve. Histamine may come into play through various channels. In this connection, we would recall the fact that microscopic examination of the pregnant uterus demonstrates that at all periods of pregnancy varying amounts of fetal ectoderm—*syncytial buds*—are constantly being cast off from the periphery of the ovum and gaining access to the maternal circulation (Fig. 16). Since such structures must eventually break down and dissolve in the blood within the intervillous spaces, or elsewhere in the maternal circulation, it is readily understandable that their split products must come into local contact with maternal tissue. Abderhalden's test is based upon this phenomenon, and Guggisberg has isolated from the placenta a chemical substance

to which the guinea pig's uterus responds in the same way as to histamine. Therefore, it might be permissible to attribute the marked venous hyperemia of the uterine wall at least in part to the local action of histamine. If this is admitted, it is further conceivable that the local production of histamine might act as a growth-stimulating agent for the uterine musculature, particularly as there is evidence that under suitable conditions it may specifically promote growth of

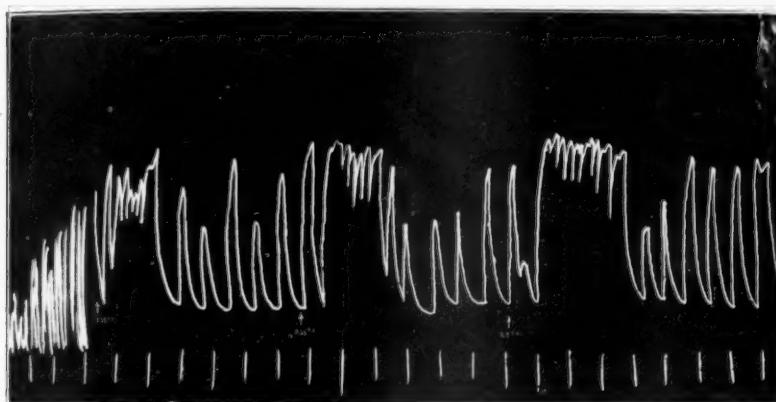


Fig. 14.—Kymographic tracing of contractions of guinea pig's uterus (half horn), after addition to Tyrode's solution of 0.25 c.c. of blood from eclamptic patient,  $\times \frac{1}{2}$  (Sun). Arrows mark time of addition.

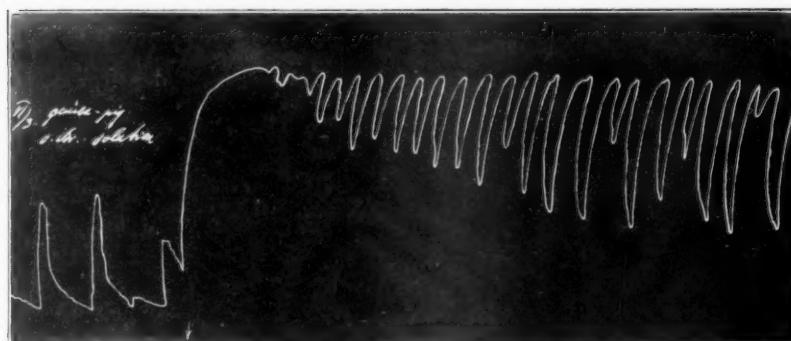


Fig. 15.—Tracing showing increase in both tonus and automatic contraction of guinea pig's uterus (whole horn) after addition of 0.0005 gm. histamine to Tyrode's solution  $\times \frac{1}{2}$ .

the genital tract (Robinson and Zondek). Again, the way by which adrenalin and pituitrin counteract the effect of histamine has already been discussed fully. Furthermore, there is another clinical phenomenon, for whose explanation no suitable theory has yet been advanced: Why does not the pregnant uterus always expel the product of conception shortly after impregnation? For under no other conditions does the uterus exhibit such tolerance to the presence of a

foreign body or an abnormal content. Not considering here the influence of the corpus luteum, the statements made by Fühner, Trendelenburg, and Nichulescu, that, after a previous dose of histamine, the uterine muscle either fails to respond to adrenalin or exhibits but a slight pituitrin effect may offer a clue towards the solution of this question.

Another area likewise concerned in the production of histamine is the posterior lobe of the pituitary body (Abel). Furthermore, it is a well-known fact that the breaking down of protein material in the intestines leads to the formation of histamine. Ordinarily, however, this does not gain access to the circulation. On the other hand, the idea has occurred to us that the protecting barrier presented by the intestinal wall may become insufficient when abnormally per-

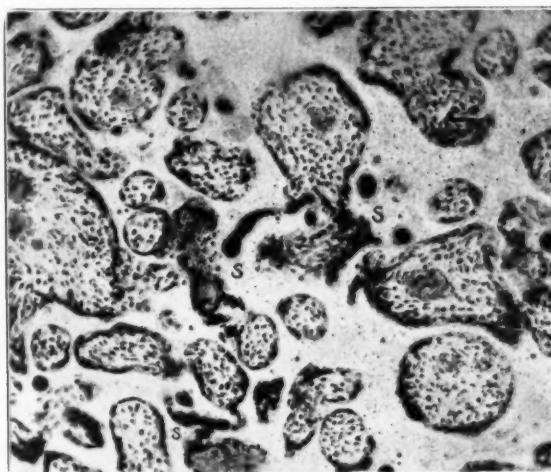


Fig. 16.—Section through human placenta at five months, showing syncytial buds.  
S., syncytial buds.

meable. We have attempted in a number of experiments to obtain information as to whether such a permeability of the intestines actually exists during pregnancy, but since these facts have not as yet been made clear to my complete satisfaction, I cannot, for the time being, commit myself to a definite opinion upon this problem. The significance of a higher degree of permeability of the intestinal wall, as a matter of fact, emerges from the experiments of McDowall and Worsnop, which show that constriction of arteries may be brought about if histamine is absorbed from the alimentary canal. "The importance of this latter observation lies in the fact that histamine is known to be a normal constituent of the intestinal content, and abnormal intestinal absorption is strongly suspected of bringing about conditions of arterial constriction in man." In this respect, it may be of interest to note that recently there exists a tendency upon the part of

internists to link up involvement of the kidneys with an abnormal absorption of amines from the intestinal canal. "It seems highly probable, from all the evidence that can be collected, that proteoses or the toxic amines, such as histamine, may be absorbed from the intestine and cause disturbances not only of nitrogenous metabolism, but also, temporarily, of renal functions" (Longcope).

#### SUMMARY

1. Following acute histamine poisoning in pregnant guinea pigs, a number of phenomena have been observed which are highly suggestive of premature separation of the normally implanted placenta as it occurs in women: the separation itself, engorgement of the vessels of the uterus and broad ligament, uterine spasm, hemorrhage into various organs, marked shock, and, histologically, edema of the uterine wall and degenerative changes in the liver and kidneys.

2. In carnivora, under similar conditions, histologic changes are produced which are suggestive of those found in women who died of eclampsia: peripheral necrosis of the liver (both of the anemic and hemorrhagic type) associated with the formation of thrombi and bile stasis, and in the kidney, degenerative changes in the epithelium of the convoluted tubules.

3. On the other hand, the administration of histamine to carnivora over a prolonged period results in changes in the liver and kidneys suggestive of those encountered in pernicious vomiting. Moreover, evidence has been adduced to show that the production of such changes can be prevented by the simultaneous administration of insulin.

4. The relation of histamine intoxication to the electrolytes in the blood, to the activity of the adrenals and the pituitary, and to the vasmotor center in the midbrain are discussed, and a possible explanation for the occurrence of hypertension is offered.

5. The striking similarity regarding blood chemistry in eclampsia and acute histamine intoxication, is emphasized, and local anesthesia is suggested as the procedure of choice in operations for premature separation of the placenta and for eclampsia. Transfusion forms an integral part of treatment in severe cases of premature separation of the normally implanted placenta. The liberal administration of oxygen—combined with an appropriate supply of glucose—is advocated in severe cases of eclampsia.

6. The possible sources of histamine during pregnancy and its biologic significance are discussed.

7. Finally, it should always be borne in mind that pure histamine and the various substances in the *histamine group*—a number of protein derivatives of unknown structure—have a similar biologic effect upon the vascular system.

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I desire to express my appreciation of the excellent work of Misses Edith Marks and Helen Lewis of the Art Department of the Johns Hopkins Medical School in the preparation of the microscopic drawings and also of Mr. O. O. Heard of the Carnegie Laboratory of Embryology in the preparation of the photomicrographs.

## THE USE OF IODINIZED OIL (IODIPIN) AS A DIAGNOSTIC AID IN GYNECOLOGY

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UNTIL a few years ago diagnoses in gynecology were made only by clinical examination and by a histologic and pathologic study of the tissues removed at operation. Pneumoperitoneum and x-ray studies of the pelvic organs, with a view of visualizing the organs were later advanced. Then Rubin perfected the technic of inflating uterus and tubes with oxygen or carbon dioxide by the vaginal route and thus gave us the best available diagnostic aid in sterility, ascertaining obstruction in the tubes, etc. It was then suggested that in cases of obstructed tubes, injection of a solution of sodium bromide, followed by x-ray examination, would exactly locate the obstruction and thus enable us to determine the best mode of treatment for curing the sterility. In some cases, however, disagreeable reactions have been reported from the sodium bromide injections, and its use has been limited.

In 1922, Sieard and Forestier,<sup>1</sup> of Paris, after much experimenting with lipiodol (40 per cent solution of iodine in poppyseed oil) and finding that it was nonirritating to the most delicate tissues, employed it for the localization of tumors of the spinal cord. In many cases

they injected 1 to 2 c.c. of lipiodol into the spinal canal seemingly without any injurious effects.

In 1923, Sergeant and Cottentot<sup>2</sup> first studied dilatations of the bronchi and bronchiectasis in adults by intratracheal injections of

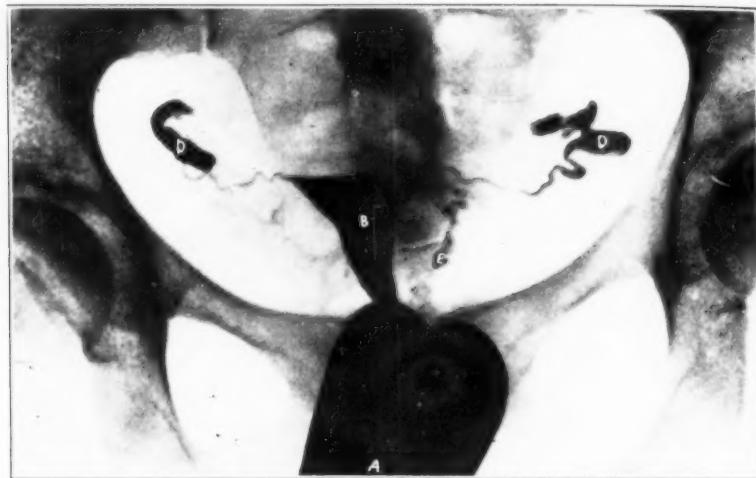


Fig. 1.—This is a case in which the uterus, tubes, and ovaries were normal in every respect. The injection was made so that one could see the size of a normal uterine cavity and tubes. It is interesting to note the extremely small lumen in the fallopian tubes. *A*, Speculum. *B*, Uterine cavity. *C*, Normal tubes. *D*, Excess iodipin—tubes open. *E*, Excess iodipin behind uterus.

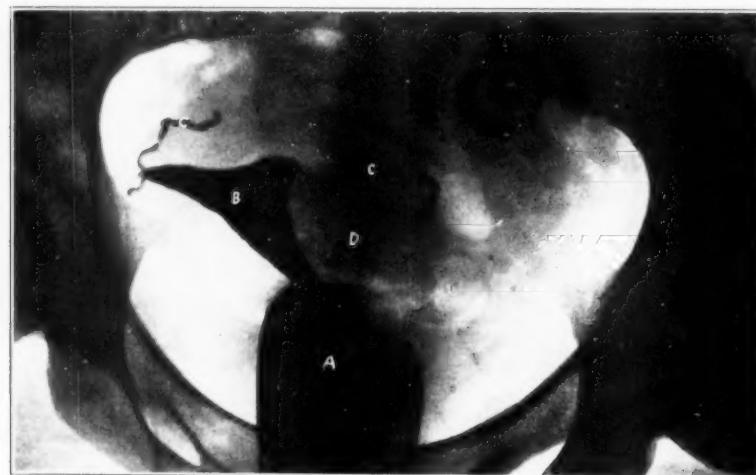


Fig. 2.—A case in which the uterus and tubes are normal. The uterus is displaced to the right of the median line by an ovarian cyst about the size of an orange, situated to the left of the median line. *A*, Speculum. *B*, Uterine cavity. *C*, Excess iodipin—tubes open. *E*, Excess iodipin behind uterus.

lipiodol through the ericothyroid membrane and reported no ill effects from its use. About the same time Armand-Delille<sup>3</sup> and his associates applied the same method in children.

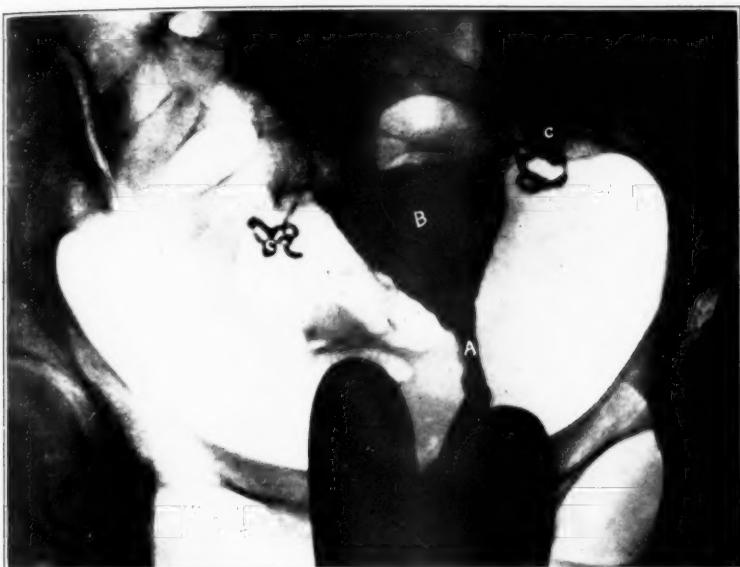


Fig. 3.—A case of chronic subinvolution of the uterus. The uterine cavity is greatly enlarged. About 10 c.c. of iodipin were required to fill the uterine cavity and both tubes. This illustrates the importance of a pelvic examination before making the injection. If one did not know the size of the uterus, he might inject insufficient solution and thus be unable to interpret the reading properly. *A*. Cervical canal. *B*. Enlarged uterine cavity. *C*. Excess iodipin—tubes open.

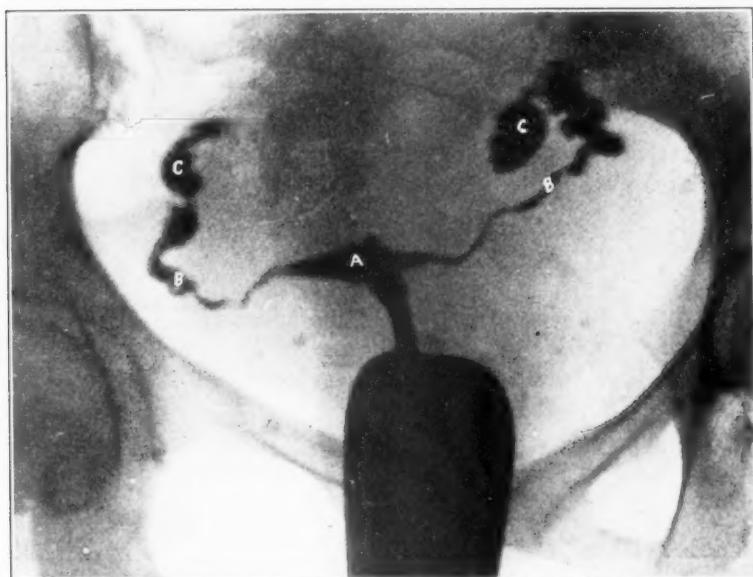


Fig. 4.—A case of acute salpingitis with pelvic abscess formation. The dilated, fimbriated extremities of both tubes denote an acute inflammatory process. The pelvic abscess was drained by vaginal section and the recovery was uneventful. *A*. Normal uterine cavity. *B*. Lumen of the tubes enlarged. *C*. Excess iodipin—tubes open.



Fig. 5.—A case of chronic subinvolution of uterus with retrodisplacement. Note the enlarged uterine cavity with some irregularities throughout. Both tubes are open. The posterior position of the uterus is not demonstrated in this picture, as it is made in an anteroposterior position. *A*. Enlarged uterine cavity. *B*. Normal tubes. *C*. Excess iodipin—tubes open.

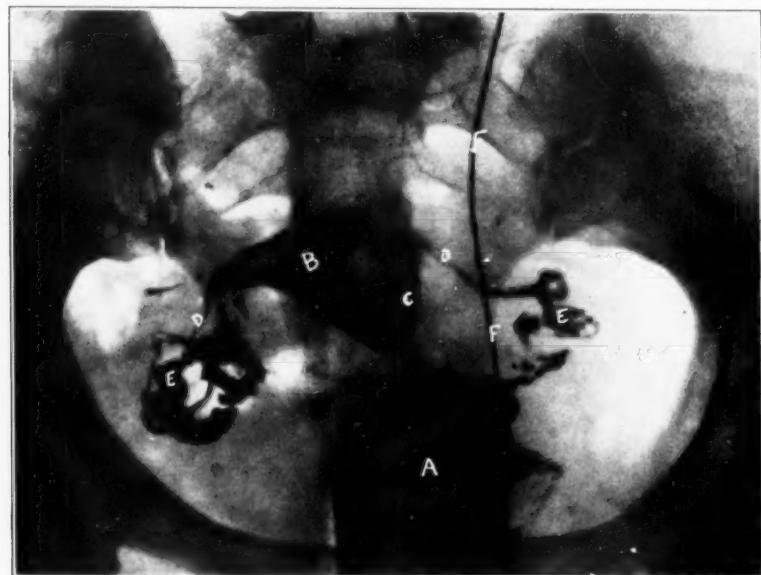


Fig. 6.—A case of a hatpin in the abdominal cavity as a result of an attempted abortion. Note that the uterine cavity and both tubes are normal in every respect. There is an excessive amount of iodipin in the abdominal cavity, as in this case too much of the solution was injected. A fistulous tract is seen where the pin perforated the uterus at its lowermost segment. At operation the pin was found imbedded along the vertebrae retroperitoneally. *A*. Speculum. *B*. Uterine cavity. *C*. Uterine sinus. *D*. Normal tubes. *E*. Excess iodipin—tubes open. *F*. Hatpin in the abdominal cavity. (An excess of iodipin was used in this case.)

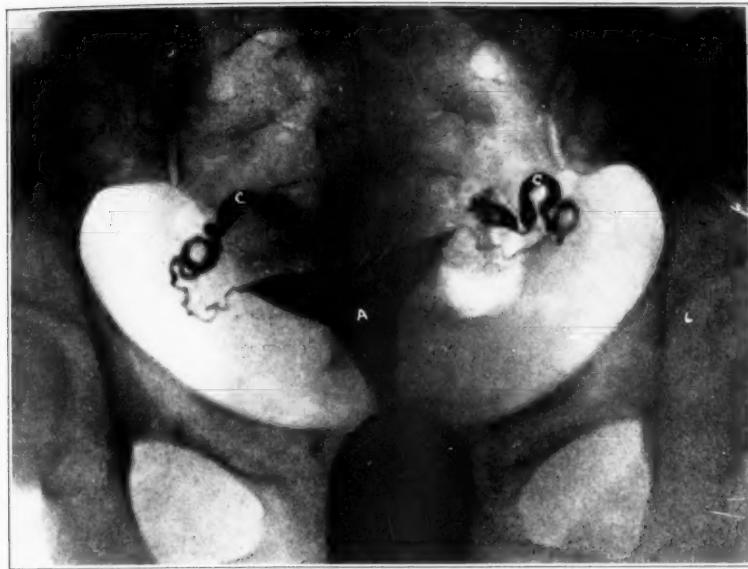


Fig. 7.—A case of pulmonary tuberculosis. Patient had tenderness about both tubes, with no history of pelvic infection, and clinically had all symptoms of tuberculous salpingitis. Both tubes show several heavy spots which may be tubercles, and if such is the case, would be very suggestive of tuberculous salpingitis. This patient would not consent to operation, and the findings were not confirmed. *A.* Uterine cavity. *B.* Tubes; note heavy spots throughout tubes suggestive of tubercles. *C.* Excess iodipin—tubes open.



Fig. 8.—Case is one of retrodisplacement with sterility. An examination of both tubes showed infiltration and fixed and clinically diagnosed chronic salpingitis. This case illustrates the value of sufficient iodipin to fill the uterine cavity and both tubes. On the right side the tube is open, and the iodipin has passed into the peritoneal cavity. On the left side the tube is closed at its end, forming a club tube. The ligaments of the uterus were shortened, and plastic work was performed on the left tube. When the club end was excised, iodipin escaped from the tube. *A.* Uterine cavity. *B.* Tubes. *C.* Obstructed left tube at infundibular portion (club tube). *D.* Excess iodipin—right tube is open.

In October 1925 David H. Ballou<sup>4</sup> of Montreal in a preliminary report on the use of lipiodol in lung conditions, stated that it was

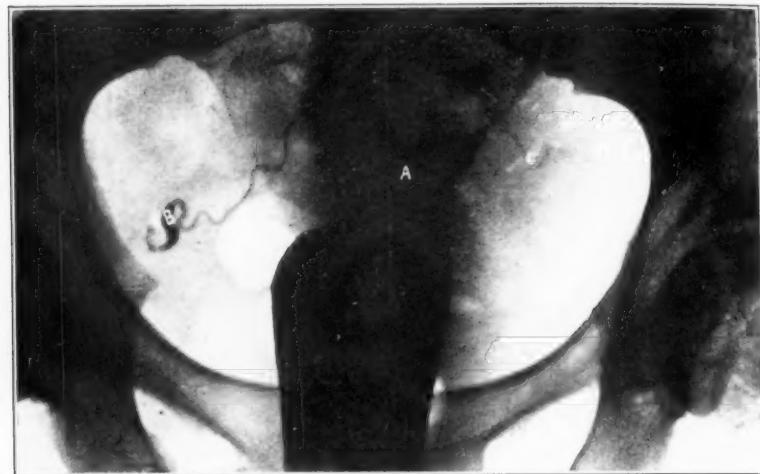


Fig. 9.—Case of subinvolution with retrodisplacement of uterus in which the right tube was open and the left tube closed. At time of operation the left tube was so badly adherent that it was impossible to do plastic work. It was, therefore, removed. A. Enlarged uterine cavity. B. Excess iodipin—right tube open. C. Obstructed left tube, partially at ampulla, completely at infundibular portion.

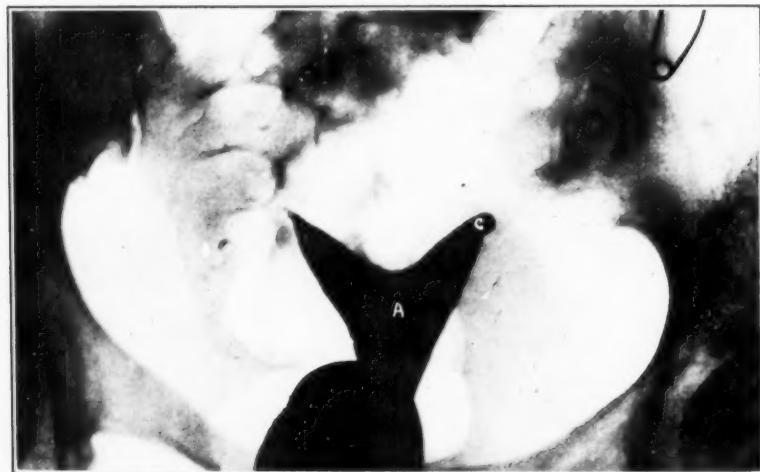


Fig. 10.—A case of bicornuate uterus with obstruction of both tubes. Illustrates beautifully the irregular uterine cavity. At operation both tubes were removed, as it was impossible to relieve the obstruction. A. Uterine cavity. B. Obstruction of right tube at its junction with uterus. Note the rounded appearance at point of obstruction on left (C).

rapidly eliminated by coughing or absorption from the alveoli, and that no ill effects were noticed.

In the early part of this year, 1926, Dr. Forestier came to this country and demonstrated his uses of lipiodol. While he was in

St. Louis, I had the pleasure of meeting him and of attending one of his demonstrations. He explained how useful in various ways lipiodol proves in the diagnosis of spinal cord and chest conditions and



Fig. 11.—A case of acute endometritis following an abortion several weeks previously. Note irregular uterine cavity with obstruction of both tubes. Immediately following the iodipin injection a curettettement was performed and the endometrium showed acute endometritis. No decidua or villi were present. Recovery uneventful. *A*. Enlarged uterine cavity. *B*. Obstruction of tubes at their junction with uterus; note the irregularity of the uterine cavity, possibly a disturbance of the mucosa.



Fig. 12.—Case of enlarged uterus with obstruction of both tubes at their interstitial portion. Note enlarged uterine cavity both in length and breadth. The uterus showed marked enlargement; a supravaginal hysterectomy with removal of both tubes was performed. The pathologist's report showed diffuse adenomyoma of uterus. *A*. Elongated and enlarged uterine cavity. *B*. Obstruction of both tubes at their junction with uterus.



Fig. 13.—A case in which the pelvis was filled with many masses, and in order to locate the uterine body an injection of iodipin was made. Note the uterine cavity elongated (A) and terminating in a broad expansion in the right side of the pelvis (B). At time of operation supravaginal hysterectomy was performed and the uterus contained many myomas, the largest of which was about the size of an orange. Such a picture helps to make a diagnosis where several masses are present, and one would like to know their origin, whether uterine or ovarian. A. Cervical canal. B. Elongated, enlarged uterine cavity.



Fig. 14.—A case of chronic salpingitis and left ovarian cyst. The pelvis in this case was blocked by a mass about the size of an orange, which extended well down in the culdesac. This was thought to be a case of fibromyoma of the uterus, but at the time of operation the large mass was found to be a left-sided intraligamentous cyst. Note that iodipin shows a normal uterine cavity with right tube normal and open at its fimbriated extremity. The left tube is prolapsed behind the fundus, and the fimbriated extremity is not seen, but there is an extravasation of the iodipin about the ovarian cyst. This is an unusual picture, and its interpretation is vague. A. Uterine cavity. B. Tubes. C. Excessive iodipin—right tube open. D. Ovarian cyst in culdesac; excess of iodipin from left tube extravasated about ovarian cyst.

showed in a few slides its application in diseases of the female genitalia, of the genitourinary tract, of sinuses, etc. I was greatly impressed by these demonstrations and immediately started to investigate its use in gynecologic patients at the Barnes Hospital.

The French preparation, "lipiodol," is rather expensive and its supply is limited in this country. Iodipin (a 40 per cent solution of iodine in vegetable oil) manufactured in this country, is readily available and not very expensive. The pictures shown in this paper are all made from injections with iodipin. So far I have failed to notice any immediate reaction and I believe that it is not irritating to the tissues of the pelvis. The legends under the illustrations give the interpretation of facts easily recognized in the pictures. In most instances the findings were fully confirmed by a later operation.

The rather simple technic employed is as follows: The patient comes to the hospital for injection and x-ray exposure, but is allowed to go home immediately after the procedure. Some few complain of

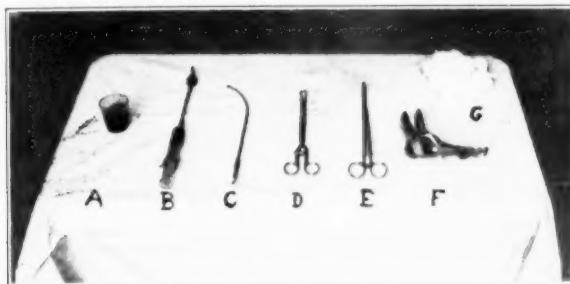


Fig. 15.—The necessary equipment for an iodipin injection. A. Tincture iodine. B. Luer syringe and cannula charged with iodipin. C. Uterine sound. D. Tenaculum forceps. E. Uterine dressing forceps. F. Graves' bivalve speculum. G. Cotton balls.

abdominal cramps during the injection; however, the discomfort lasts only a few minutes. The patient is clad in a nightgown and placed on the x-ray table in the lithotomy position. Everything is made ready for the x-ray plate, since the picture must be made as soon as the injection is finished. A Graves bivalve speculum is inserted, exposing the cervix; the field is painted with tincture of iodine, then the posterior lip of the cervix is seized with a tenaculum forceps and drawn down slightly. A sound is introduced into the uterine cavity to rule out any obstruction; the cannula (a Keyes-Ultzman urethral cannula, modified and equipped with a rubber tip which acts as a plug against the external os [Fig. 15]) is inserted into the cervical canal for about 2 cm., and firm pressure is made against the cervix. With a 15 e.e. Luer syringe, about 7 e.e. of the iodinized oil are slowly and gently injected into the uterine cavity. When it is found that the injection can only be continued under pressure, it is evident that the capacity is filled; the x-ray picture is now made. When the

cannula is withdrawn, a great portion of the iodinized oil escapes from the uterus. The patient is allowed to get up from the table, dress, and go home.

For the sake of brevity I shall not requote the various findings made; they are noted in the legends.

In the 38 cases injected in the course of three months, I have not observed one single unfavorable reaction. I had occasion to open the abdomen in 30 of these cases at various intervals, from one to fourteen days after the injections, and I have not seen any irritating effects of the iodinized oil, which has passed through the tubes, on the tissues of the pelvis. Iodinized oil apparently remains unresorbed in the pelvis for a considerable time, and this is a point to be kept in mind to avoid misleading errors if at a later time x-ray pictures are made on the same patient for a gastrointestinal diagnosis, etc. I do not feel that any chronic complications are likely to occur, since the pelvic cavity commonly proves resistant to substances even more irritating than iodinized oil. The mucosa of normal fallopian tubes, removed ten days after an injection (to sterilize an epileptic patient), revealed no signs of irritation, appearing to be normal in every respect. The time of the disappearance of the iodinized oil apparently varies greatly in different individuals. In one patient, fourteen days after an injection, the x-ray plates failed to show any remaining solution. In another individual, sixty days after an injection, there still was a small amount present in the pelvis. Most likely this is the expression of an individual factor which in one leads to quicker absorption of iodinized oil than in another. The amount injected necessarily must play a part in this respect. The exact time of disappearance of the oil from the pelvis, I was not yet able to ascertain, but I am certain the absorption is relatively quickly accomplished, and is not a matter of months, as seems to be true of injections into the spinal canal.

Summarizing my personal experience to date, I can state that iodipin injections will prove of diagnostic value:

1. In sterility cases where the tubes are found obstructed, to determine the character and location of the obstruction. It offers the welcome opportunity to decide definitely whether or not the case is suitable for operation.
2. When several masses are palpable within the pelvis. Injection and x-ray study will clearly differentiate the uterus from the other masses.
3. In cases in which the pelvis is blocked by one large mass. By this method the precise diagnosis can be made whether the tumor is originating from ovary or uterus.

4. In cases in which a foreign body is suspected within or outside the uterine cavity.

5. Iodipin injections into the uterus prove helpful in differentiating chronic appendicitis from a right-sided salpingitis, and a tuberculous salpingitis from common salpingitis, which means that they possibly might enable us to make a definite diagnosis of a tuberculous tube.

6. It is a valuable aid in indicating the size of the uterus, and in determining whether the cavity is encroached upon by any masses such as a fibromyoma, a carcinoma of the fundus, etc.

7. Iodipin injections, carefully and skillfully done, are not likely to cause any harm.

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WALL BLDG.

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#### REPORT OF A CASE OF GENERAL EDEMA OF THE FETUS FROM A RENAL ECLAMPTIC MOTHER

BY BARNARD L. LIEBERMAN, B.S., M.B., M.D., DETROIT, MICH.

GENERAL edema of the fetus, congenital fetal dropsy, or hydrops neonatorum, although of uncommon occurrence, is nevertheless not a rare entity, the literature on the subject being fairly extensive; Fordyce<sup>1</sup> alone having collected 63 cases and Hohl<sup>2</sup> having 33 cases in his series. Ballantyne gives quite an extensive bibliography, whereas Capon<sup>3</sup> has described seven individual cases of this condition. It is rather from the etiologic standpoint that this condition assumes a rôle of interest and importance, very little being known as to the etiology and pathogenesis. Many interesting and diverse theories have been advanced, but no accurate explanation has as yet been forthcoming. Of the numerous theories advanced, that of a "maternal toxemia," as first stated by Ballantyne, has received the widest cognizance. It is for this reason that this case is presented and described, it being the offspring of a mother suffering from "eclampsia," which today is the outstanding "toxemia of pregnancy" and of which so little is known from the etiologic standpoint.

Ballantyne describes general edema of the fetus as: "A rare condition of the fetus, characterized by general anæsthesia, by the presence of fluid effusions in the peritoneal, pleural, and pericardial sacs, and usually by edema of the placenta; and resulting in the death of the fetus or infant before, during or very soon after birth. It is to

be distinguished from such conditions as ascites or peritonitis of the fetus, and fetal syphilis, edema neonatorum, and congenital elephantiasis." It is also to be differentiated from the condition known as hydrops sanguinolentus fetus.

Although the literature is extensive, there are only a few cases of true general fetal edema, and yet fewer cases associated with eclampsia in the mother.

Ballantyne<sup>4</sup> gives an extensive résumé of the history of this condition, stating that Hippocrates<sup>5</sup> described a case of "fleshy fetus" or "fetus carnosus." Bourgeois,<sup>6</sup> Plater,<sup>7</sup> Severin,<sup>8</sup> Seeger,<sup>9</sup> and Dorstentius<sup>10</sup> described undoubted cases in the seventeenth century. Duttel,<sup>11</sup> De la Motte,<sup>12</sup> and Lospichlerus<sup>13</sup> each described a case in the eighteenth century. During the last seventy-five years numerous additional cases have been reported.

The etiology of this condition is not known. The primary cause has been sought in disturbances of the mother, father, or fetus or placenta.

The maternal causes are those which are generally considered as the most likely. The case herein reported is presumed to be the result of a maternal toxemia, the mother having definitely given evidence of eclampsia. Schumann in a review of 30 cases found that there was distinct evidence of maternal toxemia, namely, edema, albuminuria, and vomiting. He assumed that maternal toxins had passed into the fetal circulation, producing results of a similar nature in the fetus. Doi, quoted by Capon,<sup>2</sup> states that in the blood of pregnant women suffering from the "kidney of pregnancy" and even more definitely in that of eclamptic patients, erythroblasts may be found, and that these disappear during the puerperium; inferring that a toxin which can stimulate the maternal blood-forming organs can stimulate those of the child also.

#### CASE REPORT

Mrs. E. M. (case of Dr. W. E. Welz, Detroit), age 41 years, para iii, American, housewife. Patient entered the hospital complaining of severe headache and edema of the lower extremities. History of being 32 weeks pregnant. Past history essentially negative. Menstrual history normal. First pregnancy, 48 hours labor, forceps delivery. Child living and well. Second pregnancy, 18 hours labor, normal delivery. Child living and well. Previous puerperia normal. Patient a fairly well developed, somewhat undernourished, white woman with no marked abnormal physical findings, with the exception of moderate edema of the ankles. Blood pressure on entrance, 200/140, Wassermann and Kahn test, negative.

The urine, sp. gr. 1.020, contained albumin, 2 plus, and hyaline casts.

Blood examination showed Hb. 58 per cent, R. B. C. 3,990,000, W. B. C. 8,850, P. N. 64 per cent, S. M. 32 per cent, and L. M. 4 per cent.

P. S. P. (Renal function) Test: in 1st hour, 30 per cent; 2nd hour, 15; total 45 per cent.

Ophthalmoscopy, slight increase in the diameter of the veins. Very slight papillary edema. No albuminuric white spots.

Capillary microscopy, increased tortuosity of the capillary loops. Many serpentine forms. Slight venous engorgement. Slight stasis.

Blood viscosity, 3.2, Hess method.

During the first day at the hospital the patient had five convulsions each averaging about 90 seconds. Venesection was performed twice for a total of 750 c.c. Morphine was given for sedative effect. The following day the blood pressure had dropped to 170/110. On the third day the patient went into labor and gave birth to a stillborn fetus to be described. Delivery was normal—spontaneous. Position L. O. A. Duration of labor, six and three-quarters hours. Puerperium normal.

The heart tones were heard until twenty-four hours preceding birth. The fetus was very slightly macerated, the maceration being more marked in the photograph,



Fig. 1.

due to the action of the preservative fluid. The edema was very marked in the right shoulder and arm and in the right abdomen, as is shown in the photograph. (Fig. 1.) This was due to the position of the fetus in the uterus, the fluid gravitating to the lowest level. The length was 42 cm. and weight, 1,920 grams.

The skin was white and glistening with several blebs on the trunk. The face had a slight purple tinge. The scalp tissues contained a slightly gelatinous amber-colored fluid. The muscles were pale and edematous. The cranial contents showed some venous congestion. Cerebral tissues were glistening and edematous. A small amount of slightly turbid fluid was present. The pleural cavities were filled with a slightly opaque yellow fluid. Lungs pale pink in color; sank in water. The heart was normal. The peritoneal cavity was filled with slightly opaque yellow fluid. Abdominal viscera normal.

The placenta was found to have numerous large areas of red and white infarction with some evidence of edema. The cord was markedly edematous and had a lateral insertion.

## CONCLUSIONS

It cannot be stated definitely that there is any direct association between eclampsia and general fetal edema; in fact the two occur together rarely indeed. Wherever we do find the two states associated, however, we must consider the possibility of some third inter-linking factor being present, probably a toxic agent.

Schmidt and Moneh<sup>14</sup> have suggested the existence of an inherited capillary narrowness, which is said to be a feature of infantilism in the mother and creates the possibility of the occurrence of eclampsia. Brugsch and Hinselmann have advocated a similar viewpoint from the standpoint of the occurrence of eclampsia in the mother.

We may assume that in the case here presented, the maternal toxins may have been the causative factors in the production of the general edema of the fetus.

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#### REPORT OF A CASE OF CHORIOCARCINOMA OF THE UTERUS COMPLICATING PREGNANCY\*

By JOHN J. GILL, M.D., CHICAGO, ILL.

THIS case report is of interest on account of the patient's age, symptoms, and the pathology and condition of health one year after treatment.

Mrs. M. M., was born March 25, 1903. She was married at the age of eighteen, and has two healthy children; no miscarriages. Her past, personal, and family history have no bearing upon conditions now present.

Sept. 15, 1924, she was in good health, her weight was 135 pounds, her last regular menstruation occurred at that time. On December 15, the patient had a bloody vaginal discharge which recurred at frequent intervals during the sixty days following; on two occasions there was a profuse gush of blood. The other symptoms complained of at that time were, a thick mucous leucorrhea, severe pelvic pains, extreme loss of strength and weight, dyspnea, fainting spells, and blurred vision. On February 15, 1925, she entered Wesley Memorial Hospital; her weight was 98 pounds, red cell count, 3,600,000; white cells, 8900, hemoglobin 75 per cent, urine negative except for some pus cells, temperature 100° F., abdomen very tender but not distended. On February 16, I performed an exploratory laparotomy, removed a chronically inflamed fibrinous appendix. The large, soft, boggy uterus, completely studded over with tubercles varying from pinhead to pea-sized which did not penetrate the peritoneum, was sufficient evidence to warrant a hysterectomy.

The uterine body with a five months' fetus and other contents, removed intact, was examined by Dr. H. R. Fishback. His report showed the soft infiltrating nodules which permeated the uterine musculature to be chorioendometrioma.

Deep roentgen-ray therapy was administered by Dr. S. J. Alden, and the patient, very greatly improved in health, returned to her home on March 21, 1925. One year after her operation, she weighed 150 pounds, worked hard and stated that she felt stronger and better than ever.

\*The patient and specimens were exhibited at a staff meeting at Wesley Memorial Hospital, Feb. 5, 1926.

Physical examination showed no evidence of recurrence.

*Pathological Report.* (By H. F. Fishback, M.D., Wesley Memorial Hospital Laboratory, Chicago).—The specimen consists of the entire body of the uterus

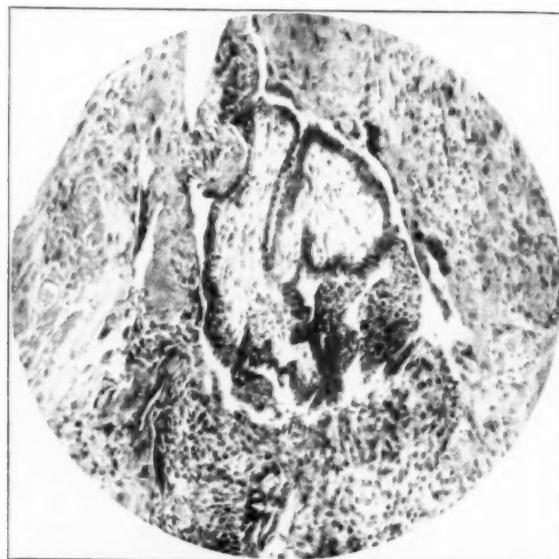


Fig. 1.—Infiltration of myometrium by tumor cells.

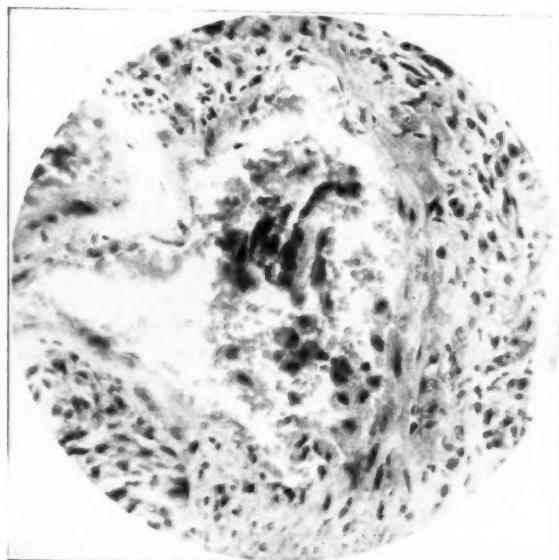


Fig. 2.—Tumor cells bound within a blood sinus.

which has been opened by a vertical cut in the anterior wall. It is symmetrically enlarged, 9x6x14 cm. and is boggy. Blood vessels are dilated and congested. There are several small yellowish, dark-red spots beneath the serosa of the upper half

of the uterus, which are fairly sharply demarcated, not elevated, and measure from 1 to 3 mm. in size. They are rather soft to the touch and upon section appear red and have in them considerable blood.

The inner surface of the uterus exhibits a thickened, soft endometrium over its lower half. The fundus portion is raw and bloody, and small bits of torn tissue project raggedly from its surface.

Sections through the wall show a heavy, soft, red muscularis containing considerable blood in widened blood channels. In the lower portion of the uterine body, the thickened endometrium can be stripped off, leaving a smooth surface. The torn fragments of the fundus are firmly attached and show extension as soft reddish-yellow bands in the myometrium. Areas of similar appearance are found irregularly throughout the wall of the fundus, but no extension outside of the uterus is found.

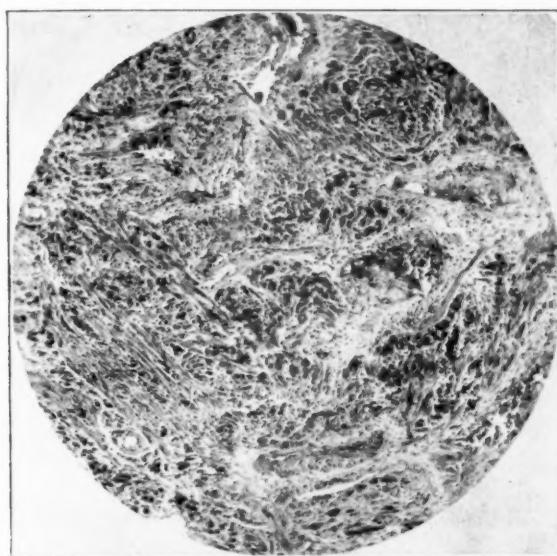


Fig. 3.—Chorionic villus showing extension of Langhans' cells into solid tissue of uterine wall.

*Histologic Examination.*—Microscopic sections of the fundus show a rough, torn inner surface. This free surface has many projecting bundles of smooth muscle fibers mingled with irregular patches of epithelial cells of Langhans' group. There is some hemorrhage on the free margin, and wide, open blood sinuses are found running to the surface.

Two chorionic villi with normal-appearing cores are found. There is no evidence of cystic degeneration as in placental moles. At the margin of these villi are found masses of Langhans' cells shown to continue as infiltrating masses in the myometrium. No covering growth of syncytium is present about the Langhans' cell masses, although there are a few irregular, small multinuclear masses of syncytium with acidophilic cytoplasm in the muscle.

The muscle is extensively infiltrated by cords and nests of Langhans' cells extending directly out into the wall, with destruction of infiltrated muscle fibers. There is no growth of tumor cells apparent along the blood channels; although there is an occasional small, loose collection of epithelial cells found within a blood sinus near the surface, it is possible that these are the cut off tips of chorionic villi.

A diagnosis of malignant tumor is established by the type of infiltration and destruction of muscle by cords and nests of atypical epithelial cells derived from Langhans' cells of the villi. Syncytial masses are few and small, and there are no inflammatory cells present, so that syncytoma need not be considered.

The placental structure which was removed was not available for examination. Chorionic villi are shown, however, with no evidence of hydatidiform degeneration.

The few villi present have cores of normal structure which indicates probably a lesser degree of malignancy, but, I believe, does not disprove a diagnosis of choriocarcinoma.

5708 HARPER AVENUE.

A STUDY OF THE BASAL METABOLISM, WEIGHT, AND  
BLOOD CHEMISTRY FOLLOWING BILATERAL  
OOPHORECTOMY\*

BY SAMUEL H. GEIST, M.D., AND M. A. GOLDBERGER, M.D.

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THERE is at the present time very little known concerning the physiology of the ovary except in its relation to the generative function. Comparatively few studies have been undertaken to determine the effect on the general metabolism after bilateral oophorectomy and most of these investigations have been carried out on animals.

Loewy and Richter<sup>1</sup> investigated the metabolic rate and stated that a definite reduction in the metabolism took place from three weeks to three and one-half months after castration. This reduction from the normal was about 12 per cent. Feeding oophorin resulted in an increase of more than 50 per cent in the metabolic rate of the castrates. It has been shown by Frank<sup>2</sup>, Geist and Harris<sup>3</sup>, and others that the various commercial extracts are physiologically inactive. Administration of these preparations fails to prevent the castration atrophy and one must be most careful in concluding that changes following the exhibition of these substances are due to their administration.

Lenethje<sup>4</sup> studied the effects on metabolism in castrated dogs and concluded that the gonads have no specific influence. He offered the suggestion that the gain in weight in women at the menopause might be due to a change in their habits. He found no definite change of any kind following castration.

Curatula and Tarueli<sup>5</sup> found a gain in weight and diminution in metabolism in a series of experiments carried out on a dog and several rats. A diminution of phosphorus excretion was also found, which is opposed to the findings of Bell<sup>6</sup> who reported an increase of phosphorus excretion in castrated animals.

McCradden<sup>7</sup> studying the metabolism in animals after castration found no general retention of the mineral elements. He also found that castration does not cause a decrease in oxidation. He pointed out that most of the experiments by other authors on the metabolism of mineral elements were not properly controlled.

\*Read at a meeting of the New York Obstetrical Society, March 9, 1926.

Aub<sup>8</sup> states that the gonads are a factor in influencing the rate of metabolism but that this role is a minor one. The removal of the gonads is followed by a slight fall in the metabolic rate.

Murlin and Bailey<sup>9</sup> carried out a series of careful experiments on two castrated dogs. They found the metabolism reduced in both animals. One, however, had had a previous thyroidectomy. Both animals gained in weight. This weight gain might have been accounted for by a lessening of muscular activity or by dietary excesses greater than their postoperative needs. The animal on whom a previous thyroidectomy had been performed, showed a less marked diminution of metabolism than the other.

Zunst<sup>10</sup> carried out a series of experiments on four women operatively castrated, who were menstruating up to the time of operation, i.e., they had functioning ovaries. Two of these women showed a diminution of metabolism seven weeks after operation. The reduction was very slight and might be considered within the limits of technical error. The other two women had fever, pain, and were ill at the time of the determinations, which factors may have influenced the results. These women showed no gain in weight. He then fed them oophorin but found no increase in the metabolic rate.

Biedl<sup>11</sup> states that the administration of ovarian extract will raise the lowered metabolism in castrated animals as much as 30 to 50 per cent above the standard obtained before operation. These results were not his own but are quotations from the literature and are made doubtful by our previously mentioned results.<sup>3</sup>

Plaut<sup>12</sup> studied five women sterilized by radiation and thus rendered amenorrheic. He investigated the basal metabolism and found a marked depression. This lowered basal metabolic rate gradually returned to normal. This latter condition he believes is due to a compensatory increased thyroid activity.

Kraul and Halter<sup>13</sup> studied five cases of x-ray castration and found a diminution of 20 per cent in the basal metabolism. They also found a weight increase at the end of three months.

Korenchevsky<sup>14</sup> found that both nitrogenous and, in most cases, gaseous metabolism were decreased after castration in fat-castrated dogs. In thin-castrated dogs the diminution was usually less pronounced or absent. The gaseous metabolism was sometimes considerably increased. He suggests the presence of specific gonadal hormones which influence body metabolism. This influence may be direct or due to secondary changes in the thyroid, hypophysis, adrenals and pancreas.

Hegar<sup>15</sup> and Keppler<sup>16</sup> studied a series of castrated women over a long period of time and found no weight increase, contrary to the generally accepted belief.

Bugbee and Simond<sup>18</sup> studied the metabolism of a castrated male dog and failed to show that castration in itself reduces the basal metabolic rate.

It will be noted that the results of the various investigations are somewhat at variance.

We attempted to study the effects of castration on the basal metabolism, weight, and blood chemistry, in order to determine if in human females living under normal conditions the removal of the gonads exerts any definable effect, also to ascertain, if possible, whether the removal of the ovaries is followed by results of sufficient physiologic importance to make it advisable to conserve them when technically possible.

We studied a total of forty-eight cases. In all of the women the menstrual function was still active before operation, so that we felt warranted to conclude that these patients were possessed of func-

tionating ovaries. In no case, as far as we could determine, was there any evidence of disease or disturbance of any other glands of internal secretion. The ovaries in some instances were microcystic.

In seven cases used as controls, three upon whom extensive vaginal plastic operations had been performed, had both ovaries conserved, the other four had one ovary left in situ.

The patients were weighed immediately before operation, after fasting eighteen hours. In addition 15 e.e. of blood was taken from the median basilic vein at this time for chemical analysis, and then the basal metabolism was determined. The process was repeated two weeks after operation and again three to five months later. Table

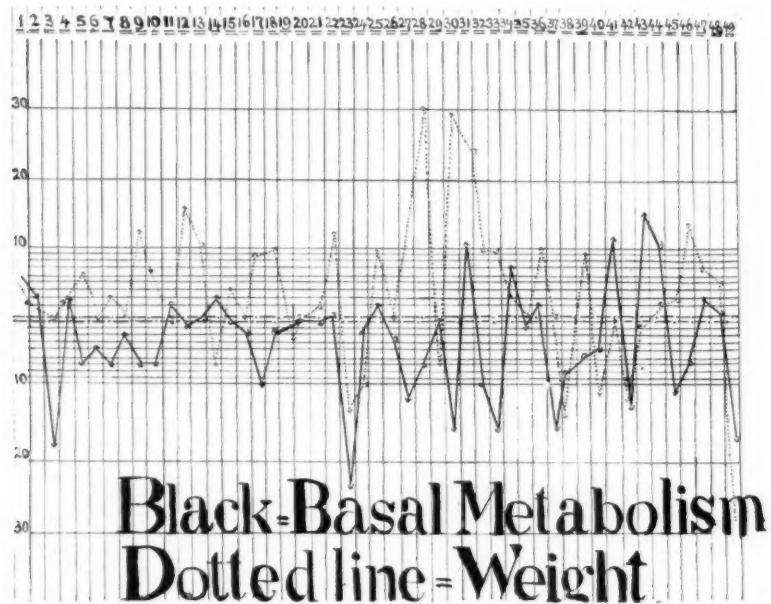


Fig. 1.—Illustrates individual cases with the basal metabolism and weight variation. The numbers at the head of the chart represent the case numbers. The double base line represents the preoperative figure, the position above the line an increase either in weight or metabolism or both, the position below the line a diminution.

The tendency for a diminution in basal metabolism and increase in body weight can be noted and the relation between weight and basal metabolism can be compared in individual cases.

I represents the weight variations up to three months after operation. We realize that the period of observation is short. Nevertheless, the tendency for weight change can be determined. It is our intention to confirm these observations on as many patients as is possible.

Several of these cases need a word of explanation. Cases 2, 3, 5 and 45 weighed over 200 lbs. before operation. These women with but one exception showed no definite cause to account for their obesity. Case 5 presented a moderate hypertrichiasis. She had a small submucous fibroid. Case 45 had a slight diminution in basal

TABLE I

	PREOP. WT.	POST. WT.	3 MONS. P. O.	DIFFERENCE
1.	145	145	140	- 5
2.	212		210	- 2
3.	260		260	0
4.	161	154	160	- 1
5.	234	242	240	+ 6
6.	150	150	150	0
7.	158	160	160	+ 2
8.	137	137	137	0
9.	115	115	127	+ 12
10.	112		117	+ 5
11.	130		129	- 1
12.	175	185	190	+ 15
13.	105	110	115	+ 10
14.	99 1/2	99	92	- 7 1/2
15.	180	185	185	+ 5
16.	160	160	160	0
17.	170	175	175	+ 5
18.	140	148	148	+ 8
19.	116 1/2		104 1/2	- 12
20.	154	152 1/2	153	- 1
21.	108	106	108 3/4	+ 3/4
22.	130		144	+ 14
23.	145		128 1/2	- 16 1/2
24.	180		168	- 12
25.	153	141	161 1/2	+ 8 1/2
26.	157 1/2	145	155 1/2	- 2
27.	157 1/2	not done	166	+ 8 1/2
28.	166 1/2	not done	186	+ 19 1/2
29.	109 1/4	99 1/4	102 1/2	- 6 3/4
30.	150	143 1/2	175 3/4	+ 25 3/4
31.	185	169 1/4	207	+ 22
32.	132 1/2	125 1/2	140	+ 7 1/2
33.	129	117	136	+ 7
34.	160	144	164	+ 4
35.	148 1/2	138 1/2	148 1/2	0
36.	156	not done	168	+ 12
37.	108	not done	108	0
38.	152	145	136	- 16
39.	153 1/2	144	162	+ 8 1/2
40.	155	142	142	- 13
41.	185	not done	185	0
42.	163 3/4	150	150	- 13 3/4
43.	131	not done	130	- 1
44.	99	97	102	+ 3
45.	216	209 1/4	222	+ 6
46.	135 1/2	125 1/4	150	+ 14 1/2
47.	170	168	176	+ 6
48.	106	105	110	+ 4

## CONTROL CASES

A	150	150	150	0
B	97	97	103	+ 6
C	168	165	165	- 3
D	148 3/4	145	148	- 3/4
E	124	114	114	- 10
F	123 1/4	116	130	+ 6 3/4
G	133 3/4	132 1/2	137	+ 3 1/4

## SUMMARY OF TABLE I

	WEIGHT GAIN	WEIGHT LOSS	NO CHANGE
Cases	26	15	7
Controls	3	3	1

metabolism (preoperative) but within normal limits. Four cases showed excessive weight changes, Cases 23, 28, 30 and 31. Case 23 showed a marked diminution in basal metabolism but a *loss* of  $16\frac{1}{2}$  pounds in weight, and Case 30 showed a marked increase in weight and a decrease in metabolism. The others presented no unusual condition to account for the weight change.

Faber<sup>17</sup> states that the tendency to accumulate fat increases as the endocrine system grows less active with advancing years. This is especially manifest in women at the menopause, although the basal metabolism is normal. If the caloric intake is above the physiologic requirement the superfluous calories throw an extra task on the organs which regulate oxidation and radiation of heat. If these organs are unequal to the task the superfluous nourishment is deposited as glycogen and fat. This metabolic anomaly may not affect the basal metabolism. This, as will be seen later, may explain why a weight increase need not necessarily signify a decrease in basal metabolism or vice versa as in Case 23.

Weight studies on patients who have returned to their homes are not entirely reliable, as many factors that influence weight, cannot be controlled after the patient has left the hospital. The physical activity (muscular), the food intake, and the psychic tranquillity have an important bearing. However, the general environment of these patients was apparently the same before as well as after operation. If any tendency exists it should manifest itself in a large series of cases and our study would indicate a tendency to weight increase. The belief, however, that castration in women is always followed by a weight increase must be modified.

In Table II we have arranged the results of the basal metabolism tests as preoperative, two weeks postoperative, and three months postoperative. The variations have been designated as minus or plus. This variation is calculated from the preoperative basal metabolism as compared with the last or three months postoperative basal metabolism.

The basal metabolism tests were conducted by Dr. Lande and the method used was as follows:

The Sanborn-Benedict apparatus was used in the determination of the basal metabolism rate, oxygen consumption alone being determined. The patients were in the absorptive state, that is about 14 hours after the last food intake, and thoroughly rested before the tests were made. Surface area was calculated according to the Aub-Dubois height-weight formula, and the normal standards of these same authors were used. In presenting these cases we wish to emphasize the necessity of great caution in interpreting basal metabolism variations. Appreciable variations in daily observations on basal metabolism are not infrequently encountered both in normal and pathologic individuals. In normal individuals the variations may amount to 10 per cent. We also wish to point out that basal metabolism determinations may be considered accurate when check observations vary less than 5 per cent.

TABLE II

	PREOP.	2 WEEKS POSTOP.	AFTER 3 MOS.	VARIATIONS
1.	35 - 3%	35 - 3%	38 + 3%	+ 6%
2.	38.6 + 8%	37 + 2	39.6 + 10%	+ 2%
3.	38 + 6%	34.5 - 5%	32 - 11%	-17%
4.	36 normal	34.5 - 5%	37.8 + 3%	+ 3%
5.	39.5 + 8%	36 normal	35.8 normal	- 8%
6.	34.7 - 3%	37 + 3%	32.8 - 9%	- 6%
7.	40 + 8%	36.8	36.8 normal	- 8%
8.	39 + 8%	38.5 + 5%	38.5 + 5%	- 3%
9.	39 + 8%	37.5 + 4%	36 normal	- 8%
10.	39 + 10%	37 + 4%	36 + 2%	- 8%
11.	36 normal	36 normal	37 + 2%	+ 2%
12.	38 + 3%	36 normal	36 normal	- 3%
13.	36 normal	36 normal	36 normal	0%
14.	35.5 normal	35.5 normal	37 + 4%	+ 4%
15.	36.5 normal	40 + 5%	36.5 normal	0
16.	37.5 + 2%	35.6 - 5%	37 normal	- 2%
17.	41 + 14%	37 normal	35 - 3%	-17%
18.	38 + 4%	36½ normal	36.5 normal	- 4%
19.	40 + 7%	--	38 + 5%	- 2%
20.	38.2 + 4%	38 + 4%	37.5 + 3%	- 1%
21.	36 normal	36 normal	36.5 normal	0
22.*	-	-	-	-
23.	44.8 + 24%	-	36 normal	-24%
24.	36.5 normal	-	35 - 3%	- 3%
25.	37.2 + 3%	37.5 + 4%	37.8 + 5%	+ 2%
26.	36 normal	35.4 - 2%	34.4 - 4%	- 4%
27.	39.6 + 10%	Not done	35.2 - 2%	-12%
28.	36 normal	Not done	34 - 7%	- 7%
29.	36 normal	36.7 normal	36 normal	0
30.	41 + 11%	40.8 + 11%	34.7 - 5%	-16%
31.	34 - 6%	Not done	37.7 + 5%	+11%
32.	37.5 + 4%	36.2 normal	31 - 14%	-10%
33.	38 + 5%	40 + 9%	31.8 - 12%	-17%
34.	34 - 7%	40 + 9%	35.8 - 2%	+ 5%
35.	36 normal	35.3 - 2%	35.3 - 2%	- 2%
36.	36.9 + 2%	32 - 11%	37.6 + 4%	+ 2%
37.	41 + 8%	36 - 4%	34 - 9%	-17%
38.	43.3 + 8%	32.5 - 9%	37 normal	- 8%
39.	33.8 - 6%	32 - 11%	32 - 11%	- 5%
40.	34.4 - 5%	36.9 + 2%	33 - 9%	- 4%
41.	34 - 6%	35.2 - 2%	37.3 + 5%	+11%
42.	38.8 + 9%	35 normal	33.5 - 4%	-13%
43.	27 - 25%	30.8 - 18%	33.2 - 9%	+16%
44.	35.5 normal	39 + 8%	40 + 11%	+11%
45.	33.2 - 9%	32 - 12%	28 - 20%	-11%
46.	37 normal	33 - 9%	34 - 7%	- 7%
47.	36.6 + 2%	28 - 20%	38 + 5%	+ 3%
48.	32 - 10%	35.2 - 2%	32 - 11%	- 1%

\*Case 22 included because of other studies on weight and blood chemistry.

## CONTROL CASES

	PREOP.	POSTOP.	AFTER 3 MOS.	VARIATIONS
A)	38 + 6%	34 + 5%	34.6 - 4%	-10%
B)	37 normal	39 + 5%	35.7 - 2%	- 2%
C)	35 - 2%	36 normal	38.4 + 6%	+ 8%
D)	38 + 5%	-	38 + 4%	- 1%
E)	42 + 15%	39 + 10%	30.5 - 9%	-24%
F)	35.5 - 2%	36.6 normal	33.5 - 9%	- 7%
G)	36 normal	-	36 normal	0

## SUMMARY OF TABLE II

	B.M. GAIN	B.M. LOSS	B.M. UNCHANGED
Cases	13	31	4
Controls	1	5	1

## CONCLUSIONS FROM TABLE II

Thirty-one cases in this series showed a decrease from 1 to 24 per cent.

Thirteen of the cases showed an increase ranging from 2 to 15 per cent.

TABLE III

	VARIATION IN BASAL METABOLISM	DIFFERENCE IN WEIGHT		VARIATION IN BASAL METABOLISM	DIFFERENCE IN WEIGHT
1.	+ 6%	- 5 lbs.	25.	+ 2%	+ 8½ lbs.
2.	+ 2%	- 2 "	26.	- 4%	- 2 "
3.	- 17%	0 "	27.	- 12%	+ 8½ "
4.	+ 3%	- 1 "	28.	- 7%	+ 19½ "
5.	- 8%	+ 6 "	29.	0	- 6¾ "
6.	- 6%	0 "	30.	- 16%	+ 25¾ "
7.	- 8%	+ 2 "	31.	+ 11%	+ 22 "
8.	- 3%	0 "	32.	- 10%	+ 7½ "
9.	- 8%	+ 12 "	33.	- 17%	+ 7 "
10.	- 8%	+ 5 "	34.	+ 5%	+ 4 "
11.	+ 2%	- 1 "	35.	- 2%	0 "
12.	- 3%	+ 15 "	36.	+ 2%	+ 12 "
13.	0%	+ 10 "	37.	- 17%	0 "
14.	+ 4%	- 7½ "	38.	- 8%	- 16 "
15.	0%	+ 5 "	39.	- 5%	+ 8½ "
16.	- 2%	0 "	40.	- 4%	- 13 "
17.	- 17	+ 5 "	41.	+ 11%	0 "
18.	- 4%	+ 8 "	42.	- 13%	- 13¾ "
19.	- 2%	- 12 "	43.	+ 16%	- 1 "
20.	- 1%	- 1 "	44.	+ 11%	+ 3 "
21.	0%	+ 3½ "	45.	- 11%	+ 6 "
22.	—	+ 14 "	46.	- 7%	+ 14½ "
23.	- 24%	- 16½ "	47.	+ 3%	+ 6 "
24.	- 3%	- 12 "	48.	- 1%	+ 4 "

## CONTROL CASES

	VARIATION IN BASAL METABOLISM	DIFFERENCE IN WEIGHT
A)	- 10%	0 lbs.
B)	- 2%	+ 6 "
C)	+ 8%	- 3 "
D)	- 1%	- ¾ "
E)	- 11%	- 10 "
F)	- 7%	+ 6¾ "
G)	0	+ 3½ "

## SUMMARY OF TABLE III

13 cases with Basal Metabolism —	{	Weight loss	— 6 cases
Rate gain showed —		Weight unchanged	— 1 case
Weight gain		Weight gain	— 6 cases
30 cases with Basal Metabolism —	{	Weight loss	— 8 cases
Rate loss showed —		Weight unchanged	— 6 cases
4 cases with Basal Metabolism —	{	Weight gain	— 16 cases
Rate unchanged showed —	{	Weight increase	— 3 cases
		Weight decrease	— 1 case

## CONTROL CASES

1 Case with Basal Metabolism — rate gain showed — Weight decrease — 1 case.	
5 Cases with Basal Metabolism —	{
Rate loss showed	
1 Case with Basal Metabolism — rate unchanged showed — Weight increase — 1 case	{
	Weight gain — 2 cases
	Weight unchanged — 1 case
	Weight loss — 2 cases

In four cases there was no change and in one the readings were missing so that a variation could not be determined.

It is well to bear in mind that the postoperative rest in bed and the following period of restricted activity would both tend to a lowered basal metabolic rate. It would be well not to conclude that the general tendency toward a reduced basal metabolism rate after castration is due entirely to the removal of the gonads. In several instances where the difference between preoperative and postoperative readings showed a marked reduction as in Cases 3, 17, 27 and 37 the individual readings were within normal limits and the difference might permit of another interpretation.

However, the fact remains that in the majority of cases studied the tendency has been for a diminution, even though 20 of the 31 cases were within the limit of technical error. It is rather significant that this technical error tended always below the normal.

It is interesting to note that there is no definite relation between the weight gain and the basal metabolism rate. In the case with the greatest diminution in basal metabolism rate of +17 per cent no weight change was noted. (Table III.)

We would not expect these relationships though Faber has offered an explanation for this discrepancy. We feel, as mentioned before, that factors other than the metabolic rate must be important in controlling the weight.

In 16 of the 48 cases, 33 1/3 per cent, there was a decrease in basal metabolism and increase in weight. These range from a basal metabolism rate loss of 1 per cent and a 4 pounds gain to a 16 per cent basal metabolism rate decrease and a 25 3/4 pounds gain. There does not seem to be any arithmetical relation between the decreased basal metabolism rate and the increase of weight, e.g., Case 28 with a basal metabolism rate loss of 7 per cent had a 25 1/2 pounds weight increase, and Case 27 with a basal metabolism rate loss of 12 per cent only had an 8 pounds increase. In six cases in which there was a basal metabolism rate diminution the weight was stationary.

Lack of conformity between basal metabolism and weight variation is not an unusual finding in metabolic studies of any kind. The great majority of obesity cases have a normal metabolic rate, and it is only in rare instances that weight increase can be explained solely on the basis of a decreased basal metabolism.

In Table IV we have tabulated the results of the blood chemistry studies. It will be seen that there are no significant variations and we are compelled to conclude that the removal of the ovaries results in no change in the blood chemistry, as determined up to a period three months postoperative, with our present method of investigation.

In Table V we have a record of pre- and postoperative blood pressure readings. These readings were taken twenty-four hours pre-

TABLE IV

Case	UREA N.			INOSAG. N.			URIC ACID			CREATININ			CHOLESTERIN				
	1st	2nd	3rd	Diff.	1st	2nd	3rd	Diff.	1st	2nd	3rd	Diff.	1st	2nd	3rd	Diff.	
1	16.8	19.6	14.0	-2.8	63.0	40.9	30.7	-32.3	5.0	1.6	0.7	-3.4	1.0	+0.3	0.188	QNS*	
2	18.2	19.6	18.2	0	50.2	42.0	35.0	-15.2	3.2	1.9	2.6	-0.6	1.5	-1.3	-0.2	QNS 0.182	
3	21.0	23.8	11.2	-9.8	54.3	54.6	35.0	-19.3	2.2	1.8	2.0	-0.2	1.2	1.0	1.4	+0.2	
4	14.0	12.6	15.4	+1.4	34.1	31.2	42.0	+7.9	4.8	2.0	2.17	-2.63	1.1	1.3	1.2	+0.1	
5	23.8	15.6	16.8	-7.0	31.5	34.1	38.5	+7.0	3.18	2.5	3.13	-0.05	1.3	1.0	1.0	-0.3	
6	23.8	22.4	**	-1.4	34.1	46.5	38.5	+4.4	5.2	2.8	2.0	-3.2	1.2	1.3	1.0	-0.2	
7	16.8	14.0	12.6	-4.2	30.9	30.7	43.3	+12.4	2.5	1.8	2.1	-0.4	1.0	1.1	1.0	0	
8	18.2	15.4	16.8	-1.4	40.0	50.9	46.7	+6.7	2.6	3.2	3.0	+0.4	1.0	1.0	1.3	+0.3	
9	22.4	21.0	11.2	-1.4	49.0	38.5	47.8	-1.2	2.9	1.5	1.7	-1.2	0.9	1.0	0.9	0	
10	14.0	16.8	15.4	+1.4	35.9	52.5	35.0	-	0.9	1.5	2.0	+0.5	0.9	1.4	1.4	+0.5	
11	21.0	21.0	12.6	-12.9	8.1	40.9	30.0	-37.8	-	3.1	1.4	2.0	+0.7	1.4	1.0	1.3	-0.1
12	25.2	16.8	15.4	-9.8	36.7	43.3	45.5	+8.8	1.9	1.3	2.3	+0.4	1.4	0.9	1.1	-0.3	
13	14.0	11.2	14.0	0	37.6	40.9	33.3	-4.3	1.5	1.3	1.7	+0.22	1.0	0.9	1.0	0	
14	21.0	15.2	12.6	18.2	23.3	30.9	32.3	37.6	1.7	1.5	2.4	+0.2	1.3	1.6	1.3	-0.1	
15	14.0	14.0	15.4	-1.4	30.7	36.7	30.7	-6.0	1.9	2.1	2.1	-0.2	0.9	1.0	0.9	0.100	
16	18	12.6	15.4	-1.4	35.0	31.5	31.5	-3.5	2.1	2.1	2.1	-0.5	0.8	0.8	0.8	0.124	
17	19	16.8	-1.2	46.0	QNS	31.5	2.5	-2.4	2.0	-0.5	1.1	1.1	-0.5	1.3	1.3	0.142	
18	20	16.8	14.0	-2.8	45.5	27.3	42.0	+10.5	4.2	1.7	1.6	-1.7	1.0	1.2	1.0	QNS 0.190	
21	21	18.2	16.8	+1.4	31.5	35.0	35.0	-7.0	3.7	2.5	-1.7	1.0	1.4	+0.4	QNS 0.136		
22	23	14.0	15.4	+1.4	42.0	42.0	42.0	-12.0	2.7	2.5	-1.2	1.1	1.4	+0.1	QNS 0.136		
24	24	QNS	16.8	35.0	35.0	35.0	35.0	-12.0	2.7	1.8	-0.9	1.4	-0.4	0.150	QNS 0.136		
25	25	12.6	18.2	+5.6	30.0	34.1	34.1	-4.1	2.5	2.1	3.9	+1.4	1.0	1.1	+0.2	-0.020	
26	26	14.0	14.0	-1.4	40.9	26.7	26.7	-6.7	2.4	2.1	4.3	+1.9	1.1	1.2	+0.1	QNS 0.136	
27	27	11.2	14.0	+2.8	30.0	43.3	43.3	+13.3	2.5	2.0	-0.5	1.0	1.1	+0.1	0.236	-0.03	

\*QNS = Quantity not sufficient for examination.

TABLE IV—CONTINUED

Case	UREA N.			INCOAG. N.			URIC ACID			CREATININ			CHOLESTERIN			
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	
	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	Diff.	
28	12.6	12.6	12.6	0	35.9	30.7	-5.2	1.6	2.3	+0.7	1.0	1.1	+0.1	0.100	0.170	
29	14.0	23.8	21.0	+7.0	30.0	46.7	51.2	2.4	1.6	3.8	+1.4	1.1	-0.1	0.226	0.146	
30	18.2	14.0	15.4	-2.8	30.0	30.0	+21.2	+2.6	1.8	2.0	+0.5	1.0	-0.1	0.294	+0.07	
31	15.4	16.0	16.0	+0.6	30.0	30.0	0	2.3	2.0	-0.3	1.2	0.9	-0.1	0.130	0.178	
32	12.6	14.0	15.4	+2.8	34.1	33.3	QNS	1.7	1.6	2.1	+0.4	0.9	1.1	-0.1	0.236	
33	12.6	14.0	14.0	+1.4	30.0	34.1	35.8	+5.8	1.5	2.5	+0.3	1.1	1.0	+0.1	0.112	
34	14.0	14.0	18.2	+4.2	36.1	32.8	2.1	2.1	2.0	-0.1	1.1	1.1	0	0.120	0.170	
35	14.0	14.0	19.6	+5.6	QNS	33.3	QNS	1.6	2.0	2.3	+0.7	1.0	0	0.130	0.176	
36	12.6	11.2	16.8	+4.2	27.3	34.1	+6.8	1.8	1.8	2.3	+0.5	0.8	1.0	+0.2	0.184	
37	11.2	12.6	16.8	+5.6	37.6	28.0	-2.6	1.8	1.8	1.8	0	0.9	0.9	0	0.190	
38	16.8	16.2	14.0	-2.8	29.3	37.6	QNS	1.6	3.1	2.3	+0.7	0.9	1.0	+0.1	0.296	
39	12.6	15.4	14.0	+1.4	33.3	38.5	QNS	2.1	2.0	2.5	+0.4	1.0	1.1	+0.2	0.188	
40	14.0	14.0	0	36.7	33.3	-3.4	2.0	0	1.8	-0.2	1.1	1.0	+0.1	0.170	0.142	
41	15.4	14.0	14.0	-1.4	30.0	30.0	0	2.3	0	3.0	+0.7	1.2	1.0	-0.1	-0.068	
42	14.0	12.6	22.4	+8.4	33.3	QNS	48.8	+15.5	1.9	QNS	1.9	0	1.1	-0.2	-0.052	
43	18.2	15.4	21.0	+2.8	35.0	QNS	30.6	+3.6	1.7	2.0	1.5	-0.2	1.1	1.0	+0.170	
44	14.0	14.0	16.8	+2.8	30.0	QNS	42.3	+12.6	2.0	2.0	1.2	1.0	1.1	0	0.160	
45	14.0	15.4	18.2	+4.2	30.0	36.7	42.3	+12.3	2.0	2.0	1.5	1.1	-0.1	0.100	0.176	
46	15.4	14.0	14.0	-1.4	QNS	32.6	33.3	0	3.5	2.3	0	1.1	1.0	+0.1	0.218	
47	14.0	14.0	0	33.3	34.1	0	2.1	2.5	3.0	+0.9	1.0	1.1	0	0.170	0.170	
48	15.4	15.4	19.6	+4.2	36.7	49.0	36.7	0	1.8	1.8	+0.7	0.9	0.9	0	0.170	-0.048
CONTROL CASES																
A	23.8	16.0	16.8	47.8	32.3	30.7	-17.1	QNS	4.4	3.0	QNS	1.3	1.2	QNS	0.150	
B	15.4	15.4	14.0	14.0	35.9	43.3	30.0	-5.9	1.2	1.2	1.2	1.1	1.1	QNS	0.148	
C	11.2	12.6	16.4	36.7	40.0	36.7	0	2.7	2.1	QNS	1.0	1.0	1.0	0.212	0.182	
D	14.0	14.9	14.0	30.0	30.8	+0.8	2.1	2.1	1.75	1.0	1.0	0.95	QNS	0.130	0.112	
E	22.4	15.4	21.0	31.5	44.4	+12.9	2.4	1.6	1.6	2.5	1.2	1.2	1.3	QNS	0.34	
F	19.6	12.6	19.6	0	39.5	QNS	40.2	+0.7	2.3	2.3	2.3	1.1	1.1	+0.2	0.124	0.182

operative, some two weeks postoperative and all again three months postoperative. Here again we found no change of significant nature and must conclude that the operative removal of the ovaries does not cause any definite change in blood pressure up to a period three months postoperative.

TABLE V  
BLOOD PRESSURE

CASE	1ST	2ND	3RD	DIFF.
25	120/80		116/96	
26	158/72		104/76	
27	125/90		112/72	
28	92/60		128/90	
29	116/78	105/60	122/108	
30	110/78	120/80	110/74	
31	118/75		120/80	
32	125/80	122/78	125/80	
33	118/68	115/60	140/90	
34	115/80	138/78	110/72	
35	105/78	90/60	110/78	
36	128/75	95/50	95/65	
37	85/60		130/80	
38	170/110	135/86	155/85	
39	120/80		120/82	
40	110/70	110/75	110/70	
41	118/75		118/70	
42	125/78	125/78	120/70	
44	105/65	110/70	110/78	
45	100/60	146/96	120/80	
46	105/60		120/80	
47	120/100	106/40	130/86	
48	120/100		98/60	

Summing up the results of our investigations it would seem that castration in women with previously functioning ovaries does not result in a consistent variation of the basal metabolism or the body weight. There seems to be no definite relationship between the variations in weight and basal metabolism. Likewise the blood chemistry and pressure remain uninfluenced.

These results may be due to (a) the inaccuracy of our present clinical methods of examination, (b) the influence of other important extraneous factors, (c) the absence of any ovarian influence.

The changes above mentioned are not of sufficient fundamental importance to warrant their being used as an argument for the conservation of the ovaries.

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(For discussion, see page 288.)

## PROBLEMS OF ORGAN CONSERVATION IN PELVIC SURGERY\*

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IN THE daily routine of pelvic surgery the gynecologist is repeatedly confronted with questions of organ conservation, the decision of which may have a most important bearing on the later welfare of the patient. The solution of these numerous problems not only involves the physical health of the patient but it must take into serious account also her mental equanimity and her domestic relationships. In certain cases in which the life of the patient is at stake the problems are simple and depend upon an ordinary knowledge of pelvic pathology. In other cases, however, in which the health of the patient is less seriously involved the problems are more complex and demand for their wise solution an understanding not only of woman in general but of the particular womanhood of the patient under treatment. Before taking up in detail the questions of operative technic in organ conservation and removal, I will, with your permission, devote the first part of this paper to a discussion of womankind in her specific relationship to her genital apparatus. The subject will be approached from two angles: first, that of the actual physical value of the genital organs to the female organism, and secondly, woman's personal valuation of her sexual apparatus.

*Physical Value of the Genital Organs.*—Our first inquiry, then, is: What is the distinctive importance of the female genital organs, severally and collectively, to the life and well-being of the individual? This seemingly axiomatic question would not by any means be uniformly answered either by the profession or the laity, and it therefore deserves a brief discussion.

During the period of childhood, that is to say, from infancy to puberty, the ovaries are the dominant factors in the genital system, for they undoubtedly play an important rôle in somatic development,

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the other organs being of passive significance. Every gynecologist has seen examples of full bodily development, even including secondary sexual characters in women with absent or rudimentary portions of the müllerian system. In their developmental capacity the ovaries collaborate with the other organs of internal secretion. Our knowledge of the true secretory power of the gonads in early life, especially that of the ovaries, is meager and at the present time practically at a standstill. But we do know that they are reciprocal or balanceing agents in their relation to other more powerful glands like the hypophysis, and that their presence is essential to normal bodily evolution. Castration, therefore, before puberty is justly regarded as an irremediable disaster and is never resorted to excepting as a life-saving measure.

During adolescence, although the genital organs have assumed the function of reproduction, the ovaries continue to exert their reciprocal influence for development, so that the necessity of castration at this period is also a serious misfortune.

Fortunately the surgeon is rarely called upon to ablate the ovaries during childhood and then only in cases of neoplasms which usually indicate some congenital defect and which have already by their growth damaged the processes of development. During adolescence the serious conditions that may occur from gynatresia or specific infections can usually be met by a wise conservatism which though it may not restore the power of reproduction, will at least preserve the ovarian and uterine functions so necessary for the full maturity of womanhood.

Most of the problems of conservation that confront the surgeon are met with in patients who have reached or passed the age of maturity, which with somewhat wide variations may be set at twenty-two years. For the solution of these problems, one must adopt a new valuation of the genital organs.

No one will deny that the genital system of a woman was designed by Nature ultimately for reproduction. It must be granted, therefore, that it is the surgeon's duty to follow Nature's purpose, and in every way consistent with the patient's health and life, to endeavor to conserve or restore reproductive power. To this obviously righteous doctrine members of the profession do not react uniformly on account of a difference of opinion as to what constitutes the welfare of the patient. Thus during a given operation a conscientious operator may adopt contraceptive measures which to another surgeon, equally conscientious, would be inexcusable. And therein lies the problem.

But in addition to the reproductive function of the genital system there is another which is less distinctive and about which there is

decided disagreement, namely, the influence on the bodily organism of the internal secretion of the adult ovary. That there is such a secretion and that it has an influence on the organism is generally accepted. But the nature and origin of the secretion and the importance of its constitutional effects are matters not so well established. The question of ovarian influence is the keynote of many a pelvic problem. Long before hormones were ever discovered it was the popular belief that the loss of ovaries doomed a woman to eunuchoid transformations, such as increased facial pilosity, deepening of the voice, masculine temperament and other changes the existence of which depended on superstitious imagination rather than on scientific fact. Nor has the fallacy completely passed. Believers in this doctrine fail to observe that a normal woman is as feminine and motherly after the natural menopause as she was before she lost her ovarian secretions, and often more so. There are still members of the profession whose character analysis cannot stretch beyond the horizon of sex, who are as firmly convinced that the nature of woman is centered in her gonads, as was Rene Descartes that the human soul resides in the pineal gland. They seem not to realize that woman is woman not only in her sexual apparatus but in every fiber of her being, in her skin, her contour, her bones, her internal organs, and above all, in her brain cells and mental processes.

Now when we come to inquire what palpable, unmistakable changes take place after the natural or artificial menopause which may be connected in a definite causal relationship with the loss of ovarian function, we find that there are only two, namely, atrophy of the other genitals, which is inevitable, and vasomotor disturbances, mostly in the form of hot flushes, which ensue in the majority of cases. Each of these conditions may be so severe as seriously to impair the patient's health, but such an outcome is exceptional and usually indicates, as we shall see later, some specific constitutional defect in the patient's make-up. Aside from these two unpleasant but comparatively unimportant sequelae, we have never been able to observe in otherwise normal women any profound physical, spiritual, or sexual changes that might be consistently ascribed to the loss of the ovarian secretion. Nor have we ever been able to identify, or even take much stock in, "ovarian deficiency" as a specific disease unassociated with other glandular or neurologic defects. It is our conviction, therefore, after many years of study of gynecologic patients, that the adult ovary though supreme as an organ of reproduction, is greatly overrated as a gland of internal secretion, and that when ovarian ablation becomes necessary it portends no great catastrophe to the patient's future happiness and well-being.

*Woman's Valuation of Her Sex Apparatus.*—We shall now turn our attention to that phase of our subject which deals with the reaction of woman to her own genital system, for it is obviously important to give some consideration to what the patient herself thinks of the loss or retention of organs which the surgeon with so little thought daily subjects to the knife. And here we are approaching dangerously near that mysterious realm, the psychology of woman, which it is said has never been satisfactorily exploited either by man or woman. Very likely that is true, but when all has been said we cannot help feeling that the mystery of woman has been exaggerated. "Varium et mutabile semper est femina," said Virgil. But her very mutability can be relied upon, and calculated in advance. Mercury is labile, but it follows certain physical laws of gravity and friction, and its motions can be accurately foretold. The chief reason why woman is so great a mystery to man is that he ascribes to her nature his own instincts, motives, and mental processes, and is thereby continually astonished that she does not react as he does to the same stimuli. Man and woman are complementary and necessary to each other, but they are far from being identical in their physical and mental composition. With this truth as a basis much of the mysteriousness and incomprehensibility of woman's nature disappears. It is not our purpose to attempt a differential exposition of female psychology, but only to allude to a few sexual reactions which may be of use to us in deciding some of the questions of organ conservation.

The maternal instinct is undeniably the most powerful agent in woman's character, but the instinct of maternity is another matter, and at least in modern civilization is comparatively feeble. If, among those of our patients who are most solicitous to become fertile, we search for the true motive of their desire, we will find, in the majority of cases, that it lies not in an overwhelming natural instinct for childbearing, but is prompted rather by the instigations of an impatient partner. In other words we find that the instinct for parenthood is stronger in the male than in the female, and for that reason the loss of procreative power is less of a disaster to a woman than to a man. There are of course numerous exceptions to this general rule. When the child is born the reaction in the father is one of pride and self-satisfaction. In the mother is awakened the supreme joy of motherhood, which far outweighs her previous fear of conception and the pains of labor.

We shall now consider the organ consciousness, or perhaps we might better term it the localized sex sensibility of woman. This, be it said, is only a small part of her general sex consciousness, a subject that would involve nearly the whole field of her psychology and one that is too broad for the scope of this paper.

In the matter of organ sensibility, normal men and women are not on the same footing. The female genital organs being concealed and normally insensible excepting under sexual excitation are not an object of contemplation unless they are diseased. The woman whose mind is riveted on her perineum or her uterus or her ovaries is classified as a neurotic. Even the clitoris reflexes are comparatively feeble. If they are very active the woman is said to have masculine attributes. If they are equal to the corresponding reflexes of even the average male, they are regarded as abnormal and as indicating at least a nymphomaniacal tendency. A patient thus afflicted is subjected to a search for some source of local irritation or of neuropathic excitability. As compared with men, normal women crave affection, attention, and admiration, sexual intercourse being rather a means than an end. Hence, it is that during active sexual life, to the majority of women an amputation of the breasts or the partial closure of the vaginal orifice is a greater calamity than the removal of the uterus and its appendages.

Woman's valuation of the menstrual function is a subject on which surgeons disagree in solving some of the problems of conservation. There is no doubt that a woman who menstruates normally looks with satisfaction on the function, troublesome as it is, as an indication of health and complete womanhood, but it is impossible to believe that any woman regards the catamenial curse in itself as anything but an unavoidable nuisance. Deficient menstruation, especially when attended with pain, is a constant reminder of incompleteness, a suggester of inferiority, a fertile producer of neuroses. Absence of menses, on the other hand, is often a relief, and is a condition to which most women soon become contentedly adapted. And yet operations are advocated in the treatment of pelvic diseases, which by preserving scanty portions of the endometrium and ovaries, maintain a meager semblance of menstruation. These mutilated pelvic reliés, with their incomplete function, seem to us to be only grim reminders of misfortune, and an incessant and prolonged irritant to the patient's nervous organization.

In our study of woman as an individual we have reached the following conclusions as a practical aid in deciding certain of the problems of organ conservation.

1. Before the age of maturity every effort should be made to preserve the full function of the pelvic organs because of their influence on general development.
2. After the age of maturity, preservation of reproductive ability is the prime consideration. If this is not possible every effort should be made to maintain the *full* menstrual function. After the age of thirty-five, these requirements become progressively less stringent.

3. If, for the welfare of the patient, reproductive ability and full menstrual capacity must both be sacrificed, complete ablation is preferable to resections and transplantations that result in the scanty semblance of menstruation.

4. The surgeon should be cognizant of the patient's personal and domestic reactions to the question of conserving her organs, and should in all cases be armed with the permission to do during the operation what in his judgment is best for the patient's future welfare.

5. If after full maturity, ablation is necessary, the patient is not unsexed in the popular sense, since sex is a universal and not simply a local physical attribute; nor are the other organs of internal secretion, excepting in unusual instances, permanently disturbed.

With this somewhat discursive introduction, we shall now take up the main topic of our paper, namely, the technical problems of organ conservation. In these problems are involved questions of reproduction, pelvic mechanics, pathology, and endocrinology. Some of the factors are simple, others combined, still others antagonistic. We shall consider them with special reference to the organ concerned and shall begin with the uterus.

*Conservation of the Uterus. Fibroids.*—The most important phase of uterine conservation is met with in the childbearing period, and the chief point at issue is that of reproduction. Fibroids are the enemies of reproductive power. They are often the cause of sterility. Associated with pregnancy they constitute a dangerous complication. If allowed to grow they may necessitate the removal of the uterus and thus prevent forever the possibility of conception. If one is willing to sacrifice fertility, the treatment of uncomplicated uterine fibroids has become one of the easiest tasks of the pelvic surgeon. The operation of supravaginal hysterectomy is so well standardized that it can be done rapidly, bloodlessly, and safely. The mortality risk is low, and the future well-being of the patient may be almost guaranteed. Furthermore, the moderate risk of the operation can in many cases be avoided by a single sterilizing dose of radium, combined if necessary, with x-ray, with the promise of a high percentage of satisfactory results. These safe resources for combating the dangers of fibroid tumors represent a great advance in pelvic surgery, and are plainly an inestimable boon. But have they not led many of us to take the easy path and to neglect our duty in respect to conserving the reproductive power of our patients? Has not the more difficult and dangerous operation of myomectomy been too frequently supplanted by the simpler but more radical procedures of hysterectomy and irradiation? In our opinion the operation of myomectomy has not been sufficiently developed. The uncomfortable convalescence and danger of rupture in later pregnancies, well-known drawbacks to the operation, have been taken too much for granted. Regarded as necessary sequels, too little attempt has been made to avoid them. In this way the operation has attained an undeserved ill repute.

In this discussion of the operation of myomectomy we do not refer to the simple enucleation of small fibroids which every surgeon does as a routine, but rather to the treatment of those larger tumors, the removal of which, either on account of their size or location, appears more or less formidable. The disagreeable results of this operation are sufficiently familiar. The convalescence is apt to be stormy, with much abdominal pain and intestinal distention, often a rapid and alarming pulse, slow recovery, and later symptoms of postoperative adhesions. Too frequently we hear of a ruptured uterus during a later pregnancy, the result of a thin, incompetent scar.

From our study of myomectomy cases we are convinced that the evil results of the operation are chiefly due to imperfect technic. The operation of myomectomy is an art in itself, and requires the best skill of the plastic surgeon. It is not a mutilation, but a reconstruction. As in all plastic surgery the watchword should be "hemostasis and approximation." Bad form in myomectomy is represented by rough scooping out of the myoma with the hand, or blunt instrument; incomplete ligature of the blood vessels; tying the final sutures too tightly in order to control bleeding; and leaving a ragged, unsightly wound. Clumsy work of this kind results in hematomas in the uterine wall with destruction of the muscle fibers, oozing of blood into the peritoneal cavity with consequent peritoneal irritation and bowel stasis, thin scars, and postoperative adhesions. In order to avoid these untoward mishaps we recommend the following technic:

First of all must be borne in mind one of the basic laws of surgery, that muscle tissue should not be compressed too tightly by sutures since the muscle fibers are thereby destroyed, and the wound eventuates in a thin, incompetent scar. Hence the incision for the removal of a good sized fibroid should be made so that the wound edges may finally be approximated with a minimum amount of tension. For this purpose it is convenient to make flaps in the manner of an amputation of the leg. After the tumor has been exposed and the plane of cleavage found, it is a temptation to rip out the mass with a few vigorous flourishes. This is a grave mistake, for after such handling it is impossible to isolate and clamp the individual bleeding points and it then becomes necessary in order to control hemorrhage to place mass sutures, which on being tightly tied compress and destroy great numbers of muscle fibers. The tumor mass should be removed slowly and carefully, every bleeding vessel being clamped as it appears. Tension on the tumor brings the bleeding wall of the uterus into view and facilitates the hemostasis. The best method for tying the vessels is to sew in figure-of-eight ligatures about the clamps, otherwise there is danger of slipping and secondary hemorrhage when the uterine wall contracts. No attempt should be made to close the wound until every bleeding vessel is conscientiously tied and the whole field completely dry. In closing the uterine wound, several layers of sutures are applied in order to divide the tension and to make the approximation as broad as possible. For closing the peritoneum we recommend the use of the subcutaneous stitch employed by E. B. Piper in his cesarean section operation, as it best insures against the leaking of blood into the peritoneal cavity. For the

shorter wounds either the single or double figure-of-eight suture may be used as it secures good approximation with a minimum knot exposure. Every effort should be made, especially when multiple enucleation is required, to preserve as far as possible the natural contour of the uterus.

Since the operation of myomectomy is designed to preserve reproductive power, the endometrium should be religiously guarded. If considerable portions of the mucous membrane must be sacrificed in the effort to enucleate the tumors, the operation loses its point and hysterectomy should be performed.

The possibilities of reconstructing a uterus after myomectomy may be learned by practice-dissection of a specimen freshly removed by hysterectomy.

*The Uterus and Adnexal Disease.*—Another question relating to the conservation of the uterus, a mechanical one, is met with in cases where removal of the adnexa is necessary, as for example in the treatment of bilateral ovarian cysts. The uterus lying free in the pelvis, deprived of its adnexa, is a superfluous organ, and usually produces general pelvic discomfort. Less trouble is encountered if it is suspended to the abdominal wall, but in general it may be accepted as a surgical principle that if the ovaries must be sacrificed the uterus should at the same time be extirpated.

*Procidentia.*—There are numerous procedures in the treatment of prolapse and procidentia which entail either a removal of the uterus or putting it out of commission as an organ of reproduction. The questions here involved are both mechanical and functional. From the standpoint of mechanics our experience leads us to believe that the most effective means of permanently curing prolapse is by the suspension method. The suspension principle can best be carried out by employing the uterus and its round ligaments as a medium of attachment. It is our custom, therefore, to conserve the uterine body even in the most extensive cases of procidentia. From the standpoint of preserving fertility and the menstrual function, we find the suspension principle the most satisfactory, as it provides both for the relief of the prolapse and for future childbearing.

*Conservation of the Cervical Stump.*—The next topic for discussion is the question of removing the undiseased cervix during a routine hysterectomy as a prophylactic measure against a possible future cancer. As Dr. Polak is the most eminent champion of complete versus supracervical hysterectomy, I will briefly review his conclusions, with which no doubt you are all familiar.

Dr. Polak in the two papers which he has written on the subject, "Incidence of Cancer in the Cervix Occurring in the Retained Stump After Supracervical Amputation for Fibroids," and "Total Hysterectomy in Fibroid Tumors of the Uterus," confines his observations to operations for uterine fibroids. He calls attention to the compara-

tive frequency of the coexistence of myomas and cervical cancer, shown by Schottländer, Spence and Noble in a series of 900 total hysterectomies to be 2 per cent. On account of this menace of malignant development in the retained cervical stump, he advocates total hysterectomy as the operation of choice in all cases of fibroids where the removal of the uterus is necessary. As to the advantages claimed for the supracervical method, namely, ease and rapidity of execution, better anatomic results, and a lower percentage of morbidity and mortality, Dr. Polak points out that they have been considerably exaggerated and do not compensate for the danger of a later cancer. In his own series of cases he finds that his mortality percentage is only 0.5 per cent greater after total than after subtotal hysterectomy.

Dr. Polak's articles on the subject like all his published observations carry conviction, based as they are on incontestable facts and extensive experience. The controversy, if there be one, is founded not on principle but on expediency, as I shall attempt to show.

In my own work I have been a warm advocate of the supracervical technic chiefly on account of its ease and rapidity of performance, and because it does not expose the abdominal cavity to possible contamination from the vagina and cervix. In carrying out this policy, however, I have had conscientious regard for the cervix. When a lacerated, inflamed, or eroded cervix is present, we have considered a cervical repair combined with a subtotal hysterectomy as better safeguarding the interests of the patient than complete extirpation. In cases of doubt, frozen sections are made from the cervical tissue and examined before the abdominal operation is undertaken.

In order to determine whether or not our method is justified by the results, I have reviewed my personal hysterectomy cases up to February 1, 1926, taken both from the Free Hospital and private records. That the review may be more comprehensive I have included not only fibroids but all sorts and conditions of pelvic disease for which the operation of hysterectomy has been deemed necessary. Coming out the endocervical canal is counted as a supracervical hysterectomy, an operation which we employ for severe endocervicitis, or in certain cases of body cancer in elderly or obese patients, and where rapidity is desirable on account of some serious constitutional disease.

SUPRAVAGINAL HYSTERECTOMIES (PERSONAL CASES)

For Fibroids		754	
Deaths	6	Mortality per cent	0.79
Causes of death: Cerebral hem.			1
Pulm. embolism			2
Peritonitis			1
Acute nephritis			1
Shock			1
			6

For All Conditions Including Fibroids.....	1399
Deaths.....	22
Mortality per cent.....	1.57
Causes of death: Shock.....	3
Septicemia.....	1
Peritonitis.....	2
Typhoid.....	1
Pneumonia.....	2
Acute nephritis.....	1
Embolism (pul.).....	4
Cerebral hem.....	1
Intestinal obstruction.....	1
Myocarditis.....	1
Secondary hem.....	1
Ligated ureters.....	1
Slow exhaustion.....	3
	22
Cancer of Cervical Stump (Personal Cases) (Known)	
Late occurrence.....	4
Not diagnosed at operation.....	1
	5
Cases Seen from Other Clinics	
Late occurrence <sup>1</sup> .....	6
Not diagnosed at operation.....	12
Doubtful.....	1
	19
Total Cases Seen	
Late occurrence.....	10
Not diagnosed at operation.....	13
Doubtful.....	1
	24

## FATALITY IN CANCER OF THE CERVICAL STUMP

Late Occurrence	
Dead.....	5
No answer.....	2
Living with recurrence.....	2
Living without recurrence.....	1
	10
Not Diagnosed at Operation*	
Dead.....	6
No answer.....	3
Living with recurrence.....	3
Living without recurrence.....	2
	14

<sup>1</sup>One of these patients was operated upon at the Free Hospital by another member of the staff.

\*The "doubtful" case is included in this list.

## COMMENTS

In collecting the above statistics it has been interesting to note a marked diminution in the number of hysterectomies performed during the last five or six years. This has been due, first, to an increase in the number of myomectomies in cases formerly treated by hysterectomy; secondly, to the substitution of radium in the treatment of uterine insufficiency and the smaller fibroids; and thirdly, to the practice of conserving the uterus in all cases of proctidinia.

In the mortality statistics of supravaginal hysterectomy both for fibroids and all conditions, we call attention to the comparatively small number of deaths from peritonitis and shock. It is from these two factors that we claim vindication for our policy in employing the subtotal operation, for we feel that the figures would have been much larger had we attempted a complete hysterectomy in all cases.

It is to be noted that of the total number of cases of cancer of the cervical stump seen, the majority probably had the disease at the time of the original operation. These undiagnosed cases can hardly be used as an argument against subtotal hysterectomy provided due care is exercised in investigating the cervix.

The list of deaths from cancer appearing in the cervical stump demonstrates the fatality in this class of cases, and constitutes a legitimate argument in favor of total hysterectomy.

When cancer occurs in the cervical stump we recommend operation in preference to radium, though we recognize that the majority of cases when seen are beyond the reach of surgery.

From these figures we may derive certain impressions, which though not in the nature of absolutely proved conclusions, are nevertheless of some value as guides to surgical conduct.

1. The mortality percentage in supravaginal hysterectomies for fibroids is low. If total hysterectomy had been carried out as a routine, we are confident that in our hands, at least, the number of deaths would have considerably exceeded the incidence of cancer in the cervical stump.

2. The mortality percentage in supracervical hysterectomies for all causes, though much higher than that for fibroids, is, nevertheless, satisfactorily low, considering the desperateness of many of the cases. In the more difficult cases we feel that a total hysterectomy would often have subjected the patient to a risk greater than that of a later cancer in the stump.

3. If total hysterectomy is to be employed as a routine for fibroids, consistency demands that it be used in all cases requiring hysterectomy, especially in pelvic inflammatory disease.

4. A patient who dies from an operation is irrevocably dead. One who survives the operation but develops a later cancer of the stump has a definite though small chance of being cured of the cancer.

Dr. Polak's work sounds a note of warning to those of us who are not ready to give up the subtotal operation. When the cervix is in doubt total hysterectomy is the operation of choice. Subtotal hysterectomy should never be undertaken unless the cervix has been subjected to careful examination and necessary treatment.

*Conservation of Ovaries During Hysterectomy.*—The next problem, conservation of the ovaries during hysterectomy, is one that I present with an apology. The subject is so hackneyed that a full discussion of it would be but a tiresome repetition of time-worn arguments. I shall, therefore, be brief in my comments.

What are the facts in the case? On the one hand competent surgeons, conscientious observers, religiously conserve ovarian tissue when possible during hysterectomy in the belief that the ovaries by themselves continue to exert a beneficial influence on the patient's organism. Statistics show that their results are good. On the other hand surgeons of equal experience, and equally conscientious in their observations, religiously ablate the ovaries during the same operation in the belief that ovarian relies may be injurious. Their statistics also show good results. There is but one conclusion that can be drawn from this situation, and that is, that in treating the average woman it makes very little difference whether in the course of a hysterectomy, the ovaries be retained or ablated, the ultimate results from both methods being excellent in a high percentage of cases. In our own work we remove the ovaries chiefly because if retained they may give later trouble, either from cystic degeneration, adhesions, or even malignant change.

Another inevitable conclusion is that normally the ovaries of an adult woman are of no great importance as organs of internal secretion. But it would be a mistake to say that they have no such influence, since an occasional hysterectomized patient is encountered who exhibits prolonged vasomotor and neurotic symptoms that appear to date from her operation. Patients of this kind are seen in both the retention and ablation groups, and it is over them that the dispute in the matter has chiefly been waged. No one has definitely proved that they are more common in one group than in the other. It is therefore a not unreasonable inference that these untoward results are to be ascribed not to the form of operation but to a particularly unstable type of female organization that is thrown out of gear by the menopause.

In this connection we must mention the effect of radium on menstruating women. In our experience we can recognize no difference between the after-results of a sterilizing dose of radium and those of a hysterectomy with ablation of the ovaries. We have been interested to note that the statistics compiled by Dr. Corseaden of the Presbyterian Hospital showing the results of radium treatment are almost identical with our own figures from hysterectomy in relation to flushes, nervous symptoms, libido sexualis, etc.

*Conservation of the Adnexa.*—Problems of adnexal conservation are based on two main principles: first, that of restoring fertility, and sec-

ondly, that of preserving the menstrual function. Operations of this kind are exceedingly interesting to the reconstructive surgeon and test his plastic skill. We shall discuss the subject first from the standpoint of relieving or preventing sterility. Of foremost importance is the treatment of the ovaries. The single layer of germinal epithelium that covers the ovaries is extremely delicate and easily desquamated. The surface, therefore, is especially susceptible to traumatisms and infections with resulting adhesions. In long-standing pelvic inflammatory cases the ovarian adhesions become very tenacious, and as the ovarian tissue is friable it is often difficult to extricate the organ from its bed without severely lacerating it or leaving valuable portions of it adhering to the pelvic wall. This does no particular harm if one's final object is a hysterectomy, but if the aim of the operation is conservative, there must be as little sacrifice of ovarian tissue as possible. It is, in my opinion, a great fallacy to believe as we were once taught that one ovary is as good as two, or that half an ovary is as good as one, or that a small bit of ovarian tissue is all that a woman requires. It is important both for reproductive and menstrual purposes that as much ovarian tissue should be saved as possible, and in order to accomplish this it is necessary to carry out the dissection with painstaking care. If the blood supply of the ovary is properly guarded, laceration, even though extensive, does no great harm since the organ can be surprisingly well restored to its original form by the exercise of ordinary plastic ingenuity. In many cases an ovary that has been implicated in an infection, especially if it be that of the puerperal or appendical type is not especially adherent but is invested with a fibrinous envelope that may completely prevent the extrusion of an ovum. Ovaries of this kind may occur in association with tubes that are pervious to insufflation. The careful removal of the fibrinous investment is sometimes the determining factor in restoring fertility.

In the treatment of retention cysts which are of such size as to require removal on account of the danger of torsion or necrosis, it is often possible by careful dissection to preserve a large percentage of the ovarian tissue even though it be well spread out over the surface of the tumor. These flattened ovaries retain their function, and may be rolled and stitched into a very respectable resemblance to their natural contour. The same principle of conservation may be applied to some of the smaller dermoids, and as we shall see to the chocolate cysts.

Conservation of the tubes is a subject technically too extensive for the scope of this paper, and we shall allude only to some of the basic principles involved. In undertaking a plastic operation on a tube, the question of patency throughout its entire length is of course of first importance and on account of the valve-like action of

the lumen at the isthmus, is better determined by insufflation from below than from above. The prospect of success is greatly influenced by the nature of the pathology, and this may, in perhaps the majority of cases, be ascertained by the patient's history and the appearance of the pelvic organs. If the obstructing adhesions are the result of appendicitis or puerperal sepsis, the prognosis is more hopeful, since the infective process is perisalpingeal, and there are excellent chances that, protected by the closure of the fimbriae, the endosalpinx is undamaged. Gonorrhea on the other hand, attacks first the tubal mucosa and is especially apt to close the opening at the isthmus in which case, naturally, plastic operations on the tube are usually futile. In the presence of tuberculous, tubal conservation is not to be thought of.

One of the unrealized ideals of pelvic surgery is the consistently successful transplantation of ovarian tissue in the horns of the uterus when salpingectomy is necessary. The few authentic cures of sterility by this means, encourage us to hope that the operation both of auto- and heterotransplantation may sometime be perfected. Such an event would mark the dawn of a new epoch in practical gynecology.

The results of conservative surgery in pelvic inflammatory disease, it will be agreed, are not always brilliant, but it is certain that the operation is somewhat in the nature of a game of skill, and that delicate dissection and precise peritonization of raw surfaces add greatly to success both in the matter of symptomatology and of restoring the possibility of conception.

Conservation for the sake of maintaining menstrual function, conception being impossible, should always be practiced when possible in treating young women, the necessity diminishing as the patient approaches the climacteric. To this there can be no dissent. But the limit to which conservatism should be carried is a matter of disagreement. My personal opinion on this subject has already been intimated in the introduction to this paper. I need only repeat that I believe that preservation of the menstrual function is desirable only if it be complete. For this purpose at least the major part of one ovary and the major part of the endometrium should be present. I can see no advantage in those operations, interesting as they are from a physiologic viewpoint, which seek to maintain the appearance of menstruation by a distant transplantation of ovarian tissue. It has been our observation that patients in whom scanty portions of ovulating and menstruating tissue have been left, are apt to undergo nervous symptoms which though delayed for a time, appear sooner or later and are often prolonged for many years. It has therefore been our maxim that the dysfunction resulting from incomplete menstruation gives more ultimate trouble than do the immediate routine menopause symptoms that follow complete ablation.

*Endometriosis.*—The last subject which we shall consider is the question of conservation in the treatment of pelvic endometriosis. It requires discussion first from the standpoint of ovarian implants (chocolate cysts), and secondly from that of the more distant implants, the formerly so-called ectopic adenomyomas. When Dr. Sampson published his first paper on the chocolate cysts of the ovary and recommended radical removal of the pelvic organs, we were somewhat disturbed because in the past though ignorant of the nature of the growths, we had treated them conservatively whenever it was feasible. A review of our cases, however, showed generally good results, and we therefore continued our practice. Dr. Sampson has since changed his views in favor of conservatism. Unless the destructive process has been too extensive, chocolate cysts can often be removed with the retention of competent portions of the ovary. Since the tubes are usually not seriously damaged such conservatism is particularly desirable. Several of our patients who previous to the operation were sterile have afterwards conceived and borne healthy children. We have not observed any definite tendency to recurrence after conservative surgery.

The treatment of extragenital endometrial implants (ectopic adenomyomas) is quite a different matter from that of the chocolate cysts of the ovary. Some of these tumors appear to be limited in their growth and are sufficiently innocent. Others, notably those of the posterior culdesae and rectovaginal septum, assume a character that is clinically malignant. Since their nature of growth is infiltrating, surgical removal does not prevent a recurrence. On the theory that the activity of an endometrioma, like that of its progenitor, the endometrium, is dependent on the ovary, we have successfully treated a number of cases by hysterectomy and complete ablation of the ovaries. Our conclusions and illustrative cases have been published in the *Transactions of the American Gynecological Society* of 1925.

For their assistance in compiling the statistics contained in this paper I wish to thank Dr. George Van S. Smith, Miss H. J. Ewin, Miss Daisy MacCormick, Miss Alberta Lundagen, and Miss Dorothy Dunn.

198 COMMONWEALTH AVENUE.

(For discussion, see page 291.)

A CONTRIBUTION OF THE BIOMECHANISM AND THE  
PATHOLOGY OF ECTOPIC PREGNANCY, WITH  
A CONSIDERATION OF SOME OF ITS  
CLINICAL PHENOMENA\*

BASED ON A STUDY OF ONE HUNDRED AND THIRTY-ONE CASES

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(Continued from July)

II. THE BIOMECHANISM AND THE PATHOLOGY OF EXTRAUTERINE PREGNANCY

The array of data furnished by the study of the above cases warrants a consideration of the following problems:

1. How closely does the biomechanism of ectopic gestation simulate intrauterine pregnancy?
2. Do purely mechanical or mechanopathologic causes of an obstructive nature really play so important a rôle in the etiology of extrauterine pregnancy as is ascribed to them; and if not what may the other factors be?
3. Is the clinical terminology, "tubal abortion" correct?
4. What is the pathologic physiology of uterine bleeding in ectopic pregnancy?

1. *How closely does the biomechanism of ectopic gestation simulate that of intrauterine pregnancy?* As soon as the intrauterine ovum is ripe for placentation it burrows its way subepithelially, enters the compact and richly vascularized portion of the endometrium, and establishes its lacunar circulation. It accomplishes the latter through the arrosion of the capillaries by the chorionic villi, thus bringing the maternal blood into immediate contact with the fetal ectoderm. The bleeding attending this process is so slight that no harm accrues to the placental circulation. Under normal conditions the chorionic villi rarely if ever encroach upon the uterine musculature, and its blood vessels are consequently spared the arroding effects of the trophoblast. As the embryo grows it lifts the overlying mucosa more and more towards the uterine cavity, which stands out in marked contrast to the rest of the uterine lining. The raised portion is termed the decidua reflexa, while that lining the uterine cavity, the decidua vera. With the still further growth of the fetus these two endometrial layers meet and fuse, and in the latter months of pregnancy they form one continuous structure.

If for some reason or other the impregnated ovule tarries too long within the oviduct, its potentialities for placentation mature, and the

\*Read before the Brooklyn Gynecological Society, and the Section of Obstetrics and Gynecology of the New York Academy of Medicine.

tubal nidation results. And just as the intrauterine egg does not stay upon the surface of the endometrium but buries itself within it, so does the tubal embryo leave the surface of the endosalpingium and find its way into the deeper structures of the tube wall. This biomechanistic principle of ovular nidation was first conceived in its true light by Füth, in 1898. Aschoff, Kühne, Werth, and many subsequent investigators verified these findings. My own inquiries harmonize with the above teachings, and not only do these principles apply to tubal pregnancies, but also to primary ovarian and to primary abdominal gestations. It is worth while to reiterate the pertinent facts concerning the mode of ovarian and abdominal nidation in this series. In the former instance, the ovum did not remain within the confines of the follicle, but penetrated beyond the granulosa boundary into the ovarian stroma and left the corpus luteum behind, as demonstrated in Fig. 36. This fact is not in keeping with the time honored teaching of Van Tussenbroek announced in 1893, that a true ovarian pregnancy must show the yellow body as a component part of the capsularis, but it is in full agreement with our recent knowledge of ovular implantation. In the abdominal pregnancy the ovum burrowed its way under the peritoneum, and began to form its nest in the walls of the adjacent viscera. We may, therefore, conclude that in a truly anatomie sense every ovular nidation is either subendometrial, subendosalpingial, subfollicular, or subperitoneal, according to the site it chose, or was forced to adopt as the point of anchorage.

If the process of nidation is alike in all types of pregnancy, why do the extrauterine forms pass from a physiologic beginning to a pathologic ending, at or about the sixth week of their antenatal life? Because the ectopic nest is inadequate quantitatively and qualitatively to harbor the growing ovum. This fact is well illustrated in the cases of tubal pregnancy. Since the endosalpingium does not suffice for the ovular implantation, the latter encroaches upon the muscularis. This only delays but does not obviate the ultimate rupture of the capsularis, which leads in most cases to the death of the embryo, and at times also to that of the host. This fact made Werth state, "Every tubal pregnancy must be considered as a malignant growth." The accumulated clinical experience since Werth's time necessitates the amplification of the original dictum, which ought to read, "Every ectopic pregnancy is potentially a pathologic condition, and should be operated upon as soon as diagnosed." The factors precipitating the tragic end of extrauterine gestations may be summed up as follows: (a) The excessive intracapsular bleeding, due to the arrosion of the blood vessels in the muscularis of the tube wall, which are much larger than the capillaries of the compacta; (b) the growing ovum, which stretches the poorly yielding envelop, and (c) the pro-

gressive weakening of the capsularis caused by the lytic action of the trophoblast. Some few cases of extrauterine pregnancy may go to term, but they are usually associated with distressing abdominal pains throughout the period of gestation, and the newborn show almost invariably some developmental defects.

*The formation of a reflexa in tubal pregnancy* was either questioned or denied by Aschoff, Füth, Kühne, Kreisch, and others. My observations prove its formation beyond any doubt. The physiology of pregnancy teaches that a reflexa is an essential and vital part of its biomechanism; it keeps the laeunar circulation within definite boundaries, and thus secures a proper exchange between the maternal and the fetal blood streams. How then have these careful observers come to take a negative stand? The only cases in which an anatomically true reflexa is lacking are those in which the nidation remains strictly intramural, and the pregnancy develops in an outward direction. (Figs. 2 and 3.) But even in these cases the destined function of the reflexa is not abandoned; it is taken up by the capsularis, formed out of the muscle and connective tissue elements of the tube wall. If the opponents of the reflexa theory would have limited their contention to this type of cases, on purely morphologic grounds, their claim might be granted, but we must not admit its absence in general. A reflexal formation may also be missed in specimens examined after its fusion with the tubal mucosa, as is illustrated in Fig. 10, which is similar to the biomechanism found in the latter months of intrauterine pregnancy. But neither of these findings justifies the denial of a reflexa formation in ectopic pregnancy. We may sum up our views on the question of a reflexa formation in tubal pregnancy as follows: All pregnancies must have a reflexa to act as a limiting membrane for the laeunar spaces in order to maintain the placental circulation; but when the anatomic conditions are such as to prevent its classical formation, the capsularis acts as a substitute. As to the reason why some tubal pregnancies develop centripetally and others centrifugally, the theory of columnar and intercolumnar implantation of the ovum may serve as a working hypothesis. The thickness or thinness of the endosalpingium may perhaps also exert an influence upon the direction of ovarian growth, the findings in Case 4 suggest these possibilities.

The *decidual reaction* in ectopic gestation forms another debatable and acrimoniously fought academic subject. Bland-Sutton and Griffiths deny its presence. Aschoff admits its formation but says, "if a decidua vera does form in the tube, it appears late—about the second month of pregnancy; that the maternal decidua serotina is either wanting in the preponderance of cases, or is only slightly developed, and that its description by many observers is erroneous, for they mistook the trophoblast for the connective tissue hyper-

plasia." Frankl and Schiller contend that the decidual formation is an hyperplastic response to an inflammatory stimulus. Robert Meyer states that "no extrauterine decidua forms without an associated or a preceding inflammation." Uleseco-Stroganowa on the other hand proclaims with equal conviction that "no decidua forms without a pregnancy." Leo Loeb produced decidiuomata experimentally by introducing foreign substances into the uterine cavity, or by traumatizing the endometrium, and the following are some of his recorded observations: "Between the second and the ninth day after rut the experiments were not successful, and between the thirteenth and the sixteenth day they failed completely. If the ovaries were extirpated or the corpus luteum was cauterized, no decidua developed; and if rut was followed by impregnation, the decidual reaction was most pronounced. In the experimental decidiuomata unassociated with pregnancy the endometrial glands did not participate in the hyperplastic phenomenon." Trankau-Reiner tested the decidual tissue of intra- and extrauterine pregnancies for glycogen, fat, oxydates, and peroxydates, and found great similarities in their biochemistry. I found decidual reactions in ectopic gestation with marked frequency, in varied amounts and in varied locations. Its paucity or total absence in some cases I ascribe, not to a failure on the part of the connective tissue elements to respond to the hormones of pregnancy, but rather to its destruction by the hemorrhages associated with the premature termination of ectopic gestation. My studies also fail to lend support to the upholders of inflammation as the prime factor in calling forth a decidual reaction in the connective tissue during pregnancy. As an illustration I can cite two cases of this series, in both of which evidences of a chronic salpingitis are present, yet the decidual reaction is very slight; on the other hand, the gravid tubes with a normal mucosa present a very pronounced decidual reaction. I have also searched for Hofbauer cells in the chronically inflamed tubes and have failed to find them, but I did find some clasmatoocytes in the gravid tubes, which otherwise appeared to be normal. In consideration of these facts it is but logical and scientifically proper to look upon the extrauterine decidual reactions in the same light as we see the connective tissue hyperplasia of the endometrium, in intrauterine pregnancy; namely, reactions due to the stimulating effects of the internal secretions of the corpus luteum, placenta, pituitary, and the other synergists dominating the generative sphere.

As to the range of distribution of the extrauterine decidual reactions, my findings correspond with those of Orthmann, A. Martin, Garkisch, and Franque, Heinecius, Pinto, Mandl and Webster. The site of greatest reaction is the placental area and the tissues in its immediate vicinity, as seen in Fig. 23, but more remote places also

show this hyperplasia. Walker, in 1887, and Dobert, in 1891, recorded decidual reactions in the subperitoneal connective tissue of the pelvis in cases of abdominal pregnancy. Schmorl found the same changes in normal gestation, which extended to the ovaries, the tubes, the omentum, the appendix, the lymph glands, and the diaphragm. Decidual reactions in the opposite tube have also been described. I can record decidual reactions in the subserosa of appendices; in the submucosa of the nonpregnant portions of the tube (Fig. 13), and in the subserosa of the oviduct at a distance from the gestation area (Fig. 24). Hofmeier found decidual reactions in the cervix, and Hofbauer in the walls of the vagina and of the urinary bladder. The blood vessel walls also form a favorite site for decidual hyperplasia. I have found it quite frequently. Fellner, Zedal, Mandl and Pinto, and Frankl and Stolper are of the opinion that this morphologic change takes place in the endothelium, while my findings point to a subendothelial metamorphosis, for in my specimens, the endothelial layer retained its normal outline and appearance; Figs. 7, 8, and 37 verify this claim. The endometrium in cases of extrauterine pregnancy shows the same proliferative alterations as if the pregnancy were located within the uterine cavity, as illustrated in Figs. 14 and 31. In the case of primary ovarian pregnancy the connective tissue in the blood vessel walls was the only place where a decidual reaction was noted. Schiller observed this change in the septae of an ovarian pregnancy. As a curious find Hofbauer reported the presence of decidual cells in the larynx during pregnancy. (This probably accounts for the change of voice noted in pregnant women.)

Synthesizing all of the above cited experimental, pathologic, and clinical data, the following dieta may be formulated: (a) The biomechanism of extrauterine pregnancy simulates the intrauterine form, in the manner of ovular nidation, in the building of a reflexa, and in the decidual reaction manifested by the connective tissues. (b) A true reflexa in the anatomic sense, is wanting in those cases in which the pregnancy remained intramural, and developed outwardly, in such cases the capsularies formed by the tube wall, played the rôle of the reflexa. It may also be missed in cases in which although the pregnancy developed towards the tube lumen, the specimen was examined after the fusion between the reflexa and the vera has taken place. (c) The theory of inflammation as a cause of decidual proliferation does not stand the light of recent biologic studies, for the extrauterine connective tissue is morphologically, genetically, and functionally (biochemically) identical with that of the uterus, and should therefore respond to the same hormones which activate the latter. Unterberg's definition of extrauterine decidua embraces this concept, it reads "connective tissue cells outside the uterine cavity

which undergo decidual changes during pregnancy." (d) The quantitative and qualitative insufficiency of the nidation bed of an ectopic pregnancy is responsible for its transformation into a pathologic condition.

2. *Do mechanical or mechanopathologic conditions of an obstructive nature play so important a rôle in the etiology of extrauterine pregnancy, as is ascribed to them; and if not, what may the other causes be?* Since the advance of cellular pathology our concept of disease is centered around and upon morbid anatomy. As a result the etiology of ectopic gestation was built upon a system of hypotheses and theories resting on inflammatory, neoplastic, or congenital bases. Each of these causes is assumed to act as a physical barrier to the onward progress of the ovum, and hence its ectopic nidation. To properly evaluate their importance we shall review briefly the various theories propounded thus far.

*Salpingitis*, of gonorrhreal, tuberculous, or coli origin, is accepted in the order mentioned, as the most frequent cause of tubal gestation. It is postulated by many authorities such as Henig, Hitschmann, Kermauner, Orthmann, Paltauf, v. Franque, Williams and others, that by the agglutination of the inflamed tubal folds, meshes are formed in which the migrating ovum is trapped, and forced to form its placental attachment within the tube. Veit took a negative stand to this theory and stated that "if simple mechanical causes such as a network formation within the tube is sufficient to hinder the ovarian migration, then every conception ought to result in a tubal pregnancy, for the mucous folds of even normal tubes are so prominently developed." Veit might have carried this idea a little further and should have stated, that if mucous folds were in any way conducive to tubal nidation, then most conceptions ought to result not only in tubal forms, but also most frequently in an ampullar type; for according to Sobotta, the mucosa of this portion forms "a complicated labyrinth composed of numerous capillary spaces." In my experience the isthmal and the ampullar types occurred with equal frequency. Furthermore, in my series of one hundred and twenty-nine cases of tubal pregnancy macroscopic evidences of inflammation were present in only 18 per cent and the microscopic findings of intratubal inflammation were very few indeed. I have stained many specimens for plasma cells for corroborative proof of gonorrhreal infection, with negative results. I have also found that in the gravid tubes with definite signs of chronic salpingitis, the nidation area failed to show this lesion; giving the impression that the ovum refused to implant itself on an unhealthy soil. The specimens with fully developed reflex showed normal mucous folds on the maternal surface. All these observations indicate that the theory of inflammation and agglutination

of the tubal folds as a cause of tubal pregnancy, is not as tenable as its promulgators claimed.

Veit, Depaul, Hohne, Phillips, Schroeder, and others, believe that the loss of the ciliated epithelium in the diseased tubes, is a far more potent factor in the causation of ectopic pregnancy than the reticular formation of its folds, for the following reasons: (a) because they fail to propagate the ovum onwards, and (b) because their absence favors or hastens tubal nidation. Pinner, in 1880, and Werth, in 1904, discredited this theory by finding active ciliary motion in fresh specimens of ectopic pregnancy close to the gestation site, and also in acutely inflamed tubes. I can substantiate these facts, for many of my specimens show a well retained ciliary covering.

*Adenomyosalpingitis* as an etiologic factor of tubal pregnancy was also accepted by many authorities; firstly, because this lesion is supposed to represent the end-result of chronic salpingitis, and secondly, because it is believed to form a mechanical hindrance to the ovarian migration. Regarding the pathogenesis of adenomyosalpingitis, I have expressed my views in a previous publication (*Surg. Gynec. and Obst.*, July, 1925), and shall therefore not indulge in reiteration, but I do wish to state now, that in the few instances in which I have encountered this lesion, in association with tubal pregnancy, it bore no relation to the pregnancy, as proved by the total freedom of these gland spaces from any products of gestation.

*Tubal diverticulitis*, congenital or acquired, constitutes another theory of tubal pregnancy. Füth, Hufmann, Hohne and Kramer, Micholitsch, and Andrews, laid great stress upon this anomaly as a cause. A careful perusal of some of these communications convinced me that they are mainly repetitions of previously recorded statements and not the result of personal experience. Veit discarded this theory. My experience is limited to one but very instructive case. In Figs. 4 and 5, a wide-mouthed diverticulum is seen communicating freely with the tube lumen, and yet the ovum did not lodge in it, but in the tube wall opposite to it.

I have thus far enumerated the intratubal structural changes which are assumed as causes of ectopic gestation, and I shall now consider the extratubal conditions which are supposed to contribute towards this pathologic state.

*Bands and adhesions* were present in 6.25 per cent of my cases, but I have no criteria to prove the authenticity of these lesions as the cause. In the vast majority of my cases the serosa of the pregnant tubes was smooth and glistening.

*Ovarian tumors* pressing or distorting the tube lumen were accepted as etiologic factors, by L. Fränkel, Rosenstein, Arnold and many others. My experience with this lesion as an associated factor, is limited to two instances, but in neither of these cases did the ovarian

tumors indicate by their location that they had in any way compromised the permeability of the oviduct.

*Uterine myomata* as causes of tubal pregnancy are claimed by Buehe, Bubenhofer, Frazier, Fabrieus, Poorten, Wagner, and others. I have encountered this complication in 3 per cent of my cases, in two of which I can state with certainty, that the fibroids did predispose to a tubal nidation of the ovum.

*Developmental anomalies* of the tubes and the uterus are also described by many authorities as a possible cause of extrauterine pregnancy; I have had no experience with this condition, and I cannot evaluate its significance.

Analyzing critically all of the above enumerated theories of extrauterine pregnancy, which are recited perennially by many teachers, with the solemnity of a prayer, I am constrained to state, that most of them have grown hoary with the moss of tradition. It is true that in some few cases they may find ready application, but how are we to account for the vast and preponderating number of ectopies, in which neither macroscopic nor microscopic structural changes exist? Is not disease the result of functional disorders as well as of organic changes and if so, why not turn to the functional disturbances of ovular transportation and nidation for a solution of this problem?

How is the ovum transported from the fimbriated end of the fallopian tube to the uterine cavity? When we contemplate the fact that the ovum is constantly growing larger and larger from the moment it sets out on its journey, although when it reaches the isthmal portion its size diminishes somewhat, through the loss of the granulosa covering, and that the caliber of the tube is correspondingly becoming narrower and narrower the nearer it approaches the uterus, our faith in the physical possibility of the delicate hair-like projections covering the tubal epithelium, to accomplish this task, is justly shaken. A far more potent force than the one inherent in the cilia is needed to propel the ovum onward, and this force and power resides within the healthy tube wall, which manifests peristaltic properties.

Grosser has shown that soon after the ovum has entered the tube lumen peristaltic waves set in and the oviduct begins to undergo rhythmic dilatations and contractions which respectively accommodate and propel the growing ovum. This act may be compared to the peristaltic function of the gastrointestinal tract, or to the contractions and relaxations of the uterus at the time of labor.

Sellheim confirmed this view, and offered the following reasons in its support: "Wherever mucous folds are found in the body, a functional phase must be expected, and it is usually performed. And whenever a tubular organ is provided with an outer longitudinal and inner circular layer of smooth muscle fibers, it always manifests

rhythmic contractions and dilatations." The fallopian tubes fulfill these structural requisites and are hence capable of carrying out the corresponding physiologic function of peristalsis.

The many clinical observations made of late, during tubal insufflation add considerably to the correctness of Grosser's and Sellheim's dieta about tubal peristalsis. Rubin wrote, "Occasionally in a non-patent case, that is, where the pressure is high, we are ready to consider that the patient has occluded tubes, but on second examination we will find that the gas goes through." This fact must be interpreted as a spasmody and temporary contraction of the tube. Peterson and Cron performed a laparotomy on a patient whose tubes prior to the operation were supposed to be closed, but when the insufflation was carried out under anesthesia, the gas was seen escaping from the fimbriated ends. This clinical experiment serves as a conclusive demonstration of the contractile and expansile properties of the tube and of its subordination to psychic influences. Kennedy in his studies of dysmenorrhea and sterility, also noted spasmody contractions of the isthmial portion of the tube, which he could call forth by the injection of fluids. The peristaltic property of the tube is, therefore, no longer a mere theoretical fancy, but a definitely established physiologic fact. This phenomenon may be called forth by organic or inorganic substances finding their way into the tube lumen, or indirectly through psychic influences transmitted by the vegetative nervous system.

The ovum acting as a relatively foreign body within the tube lumen, stimulates the latter to peristaltic action, and the process of transportation is thus accomplished; the ciliated epithelium plays a very minor rôle, if any, in this function.

*What condition may interfere with the normal peristalsis of the fallopian tubes?* The proper functioning of any contractile organ depends upon a proportionate distribution of its muscular and connective tissue components, properly innervated. There are times in the life history of the generative system when the connective tissue constituent predominates, and it is considered as a normal condition. These are the prepubertal period, and the menopause. Should this developmental phase prevail during adolescence and maturity, a condition of congenital fibrosis, or as Sellheim terms it "fibromyotosis" arises, which is in all probability due to an ovarian and pituitary dysfunction or hypofunction. A tubal fibrosis may also be the sequelae to a preceding salpingitis, but it does not matter whether this excess of connective tissue in the tube walls is of a congenital or of an acquired origin; its effect upon the contractile and expansile properties of the tube, is the same; namely, diminution or a loss. This fibrotic state may also involve the uterus and the vagina, giving rise to sterility and dyspareunia. There are two sources contributing to, or interfering with, the function of the tube as a forwarding agent

of the ovum, (a) a congenital or an acquired fibrosis, and (b) a disturbed vegetative innervation.

*Can we influence these functional disturbances of the tube therapeutically?* The tubes with a poorly endowed musculature, or those with an acquired fibrosis, are beyond the range of our therapeutic aid; but those whose spasticity is due to psychic disorders, should be treated. Realizing that autonomic stability depends upon a proper potassium and calcium metabolism, which influences respectively the vagus and the sympathetic nerves, we ought to aim toward a restoration or maintenance of this chemical balance whenever disturbances of the vegetative system arise. The sympathetic tonic individual with her genital organs in a constant or recurring state of spasticity, lacks potassium or has an excess of calcium, for the sympathetic contracts and the vagus relaxes the tubes, the uterus, and the vagina. If we can bring about an equable sympathetic and parasympathetic innervation of the genitalia by proper medication, the hypertonicity of these organs ought to be relieved. Let us hope that a proper application of this form of therapy may yield satisfactory results in some forms of infantilism and sterility, and that it may also serve as a prophylactic for ectopic pregnancy.

Visualizing the etiology of tubal pregnancy from the functional viewpoint, the hitherto unexplainable occurrence of pregnancies in tubes which macroscopically and microscopically appear to be normal, finds elucidation. To some, these newer ideas, suggestions, and hypotheses may sound fanciful, but they are spun out of tested scientific threads, and all that is necessary to complete the weaving of this fabric, is to apply these academic facts to practice.

Besides the failure of the carrier to bring the passenger to the point of destination, the passenger himself may also be responsible for his halting in byways which ultimately prove to be dangerous retreats. We know now that the site of predilection for the meeting and union of the male and female pronuclei is the fimbriated end of the tube. Under normal conditions, according to the researches of Hohne and Behne, Grosser, Sellheim, and Biedl, Peters and Hofstatter, the transtubal migration of the ovum is completed in about ten days, and after its sojourn in the uterus for four more days, placentation takes place. This prolonged passage has a purpose, it permits the host and the guest to make proper preparations for an intimate and successful meeting. Should conditions arise which hasten the process of placentation before the ovum has reached the uterine cavity, such as an increase in the local temperature, or an increase in the supply of oxygen, as was proved experimentally by Hertwig and by Holt-hausen, the trophoblastic blastomeres develop precipitately and any part of the genital tract may be adapted as the nidation point. An

extrauterine pregnancy may therefore also be caused by a premature ripening of the placentation properties of the ovum, before the tenth day of its travel is over.

The above survey of all the possible causes of extrauterine pregnancy leads me to their classification in the following order of importance: (a) functional disturbances of the tubal peristalsis, of a congenital, inflammatory, or psychic origin; (b) a precocious development of the properties of nidation in the ovum, and (c) mechanical or mechanopathologic causes of an intra- or extratubal nature, which are assumed to act as physical barriers to the progress of the ovum.

(3) *Is the clinical terminology "tubal abortion" correct?* The abdominal surgeon finding a gravid tube with an apparently intact surface, from whose fimbriated end blood is escaping or a blood clot protruding, terms the condition, tubal abortion. He draws this inference from his knowledge of the pathology of uterine abortion, but are the processes alike? The termination of an intrauterine pregnancy, immaterial at what period in the course of the gestation, is brought about by two invariable factors; (a) the separation of the placenta from the compaeta, through rhesis in the uteroplacental area, and (b) through a contraction of the uterus, causing a disproportion in the uteroplacental surfaces, which hastens the separation and expulsion of the products of conception. In a tubal pregnancy, the chorionic villi have their roots deeply implanted within the muscularis of the tube wall, resembling to a certain extent, the chorionic invasion of the uterine wall in chorioepithelioma, or the type of placenta acerata; so that their separation from the tube wall in the uterine sense, is anatomically impossible. Nor can the products of pregnancy escape from the tubal lumen by virtue of an expulsive power, for the portion of the tube involved in the gestation area has lost its property of contractility, as proved by Martin, Prochownik and others. They escape because the capsularis, the reflexa, or whatever limiting membrane may have surrounded them, was destroyed; they fall out, or are possibly flooded out by the free blood in the tube lumen. These facts also prove the fallacy of leaving the affected tube *in situ*, after having squeezed out its contents, as is advocated by some, for such tubes will continue to bleed as long as the chorionic villi imbedded in their walls remain alive, and active. How are we then to interpret the bleeding from the fimbriated end of the outwardly intact pregnant tube? As stated previously the death of the ectopic ovum, is caused by the excessive intralaeunar hemorrhage, which stops the placental circulation and ultimately causes a rupture of the ovarian envelop, thus permitting the blood from the intervillous spaces to escape, through whatever avenue the chorionic villi have laid open. If the capsular rupture was internal, the blood will escape into the tube lumen and then into the abdomen through its fimbriated end; if

the rupture is external, i.e., if the nidation is intramural and the development proceeded centrifugally, the blood will flow directly into the peritoneal cavity, without invading the tube lumen; when the rupture is double, i.e., external and internal, the gestation products escape through both openings; and in some few instances the hemorrhage remains strictly intracapsular in type, and no free blood is found outside the gestation sac. In the face of these pathologic facts the hitherto employed terminology "tubal abortion" for the type of cases just described, as well as the designation of "unruptured tubal pregnancy" for cases which terminated without the escape of the gestation products from the tube, should be discarded. In their stead, I propose the following nomenclature for the various terminations of tubal pregnancies: (1) intracapsular rupture; (2) external rupture; (3) internal rupture; (4) a combination of 3 and 4.

4. *What is the pathologic physiology of uterine bleeding in ectopic pregnancy?* Since our social system and not the natural laws of sexual maturity dictates and determines conception, the vast number of ovulating follicles and their corresponding corpora lutea are doomed to untimely involution, and the uterine lining to the periodic shadings associated with bleeding, termed menstruation. Due to the frequent recurrence of this phenomenon in the human female, and its comparative freedom from harm to the general health, it is looked upon as a normal function. During the premenstrual or pregravid state, and during pregnancy, this form of bleeding does not take place; because the ovule and later the ovum is alive, and the corpus luteum continues to blossom. These are fundamental principles in the physiology of pregnancy, irrespective of its location. Uterine bleeding in ectopic gestation is therefore due to the death of the ovum, and to the simultaneous suspension of the inhibitory function of the corpus luteum, which begins to involute. Novak and Darner, of the Johns Hopkins School, entertain the same views. Polak's teaching is diametrically opposite, for he states that "the vaginal bleeding in ectopic pregnancy persists as long as the ovum is alive and partially attached to its tubal bed." In support of this postulate he cites the fact that in some cases of tubal pregnancy with intraabdominal bleeding, uterine bleeding was absent, meaning to imply that the former condition signified ovarian death. These teachings are not in keeping with the more modern knowledge of the pathologic physiology of pregnancy. The intraabdominal and the uterine bleeding associated with extrauterine pregnancy are two independent processes, each having its own pathologic background. The former is purely mechanical, caused by the erosion of the tube wall, or any other maternal tissue serving as the nidation bed, by the chorionic villi; while the latter is of a functional nature, and is due to a suspension of the inhibitory forces exerted upon the uterine mucosa, by

the living ovule or ovum, and by the corpus luteum of the pregravid or gravid states. We must also be wary in interpreting intraabdominal bleeding as a sign of ovarian death for it does not always signify it, as evidenced by the cases of intraabdominal pregnancy going to term, and which are always accompanied by intraperitoneal bleeding. We find an analogue to this pathologic condition in the intrauterine pregnancies which go to term, and which are associated with moderate concealed or open placental hemorrhages. Not even the clinical observation of uterine bleeding in full-term abdominal pregnancies is confirmatory of the contention that the living ovum calls it forth. It is not at all an uncommon experience in our practice to observe repeated menstrual cycles during the early months of normal intrauterine pregnancy; this is due to anomalous ovulations, and not to the viable or living embryo. This phenomenon will recur as long as the uterine cavity will remain partly open, i.e., up to the time when a complete union between the decidua reflexa and the vera takes place. In cases of abdominal pregnancy with aberrant ovulations the menstrual or pseudomenstrual phenomenon may continue throughout the entire period of the gestation, for in the latter instances, the uterine cavity does not become obliterated, due to the absence of a reflexal formation.\* Leaving out of consideration the rare and exceptional instances, we may postulate it as an invariable physiologic law, that uterine bleeding in association with extrauterine pregnancy, always indicates ovarian death, and a concomitant involution of the corpus luteum of pregnancy.

The supposition made by Veit long ago, and recently revived by Polak, that the source of uterine bleeding in tubal pregnancy, particularly in the interstitial variety, is due to drainage of the intratubal contents into the cavum uteri, must also be combated, for it does not stand the light of modern physiologic and clinical knowledge. Guthmann of the Seitz Clinic, demonstrated with tubal insufflations that, at or about the menstrual period, the hyperplastic decidua occludes the uterine end of the tube to such an extent, that it becomes impervious to the passage of gas. Sellheim succeeded in overcoming this resistance by using pressure amounting to 250 mm. of mercury. It is also a well-established clinical fact that no impregnation takes place at this time or during pregnancy, on account of the extreme endometrial hyperplasia which seals the tubouterine communication; the cases of superfetation excepted. Now if neither spermatozoa, nor air can pass through this physiologic barrier, during the pregravid states, how is it plausible to expect that much coarser substances like clotted blood or trophoblast can traverse it? Further-

\*The same phenomena may be observed in cases of uterus didelphys in which the nonpregnant half menstruated during the entire period of gestation, as I have observed in two cases.

more, we also know that the gravid tube is deprived of its peristaltic powers, so that no *vis-a-tergo* exists, and that the gestation products in themselves have no inherent motility. This theory of a reflux of tubal blood into the uterus, I am constrained to state, seems to be as purely hypothetical, as the one advanced by Sampson in relation to the regurgitation of uterine contents into the tubes during menstruation.

### III. A STATISTICAL AND CLINICAL ANALYSIS

A statistical study of my cases, and its comparison with the statistics of other clinicians, furnishes a number of interesting data for our consideration:

*Mortality.*—In my series the death rate was 0.7 per cent. My only fatality might have been avoided had drainage been instituted. This patient was ill at home for several weeks prior to her admission to the hospital with a slowly progressing intraabdominal hemorrhage secondary to a tubal pregnancy, running a febrile course. Within twenty-four hours following the operation, she became maniacal, the temperature rose to 107° F., and at the end of the twenty-eight hours, death ensued. From the postoperative course it can be inferred, that the operative trauma slight as it might have been, converted the already present infectious organisms into a most virulent type, with a fatal termination. In Engelman's statistics of thirty-seven cases of infected hematocoele, the mortality reached 24.4 per cent.

*Drainage.*—Although drainage might have saved my fatal case I am nevertheless averse to it as a routine procedure, whether abdominally or vaginally. I am convinced that the intact peritoneum is far more capable of caring for the infectiousness of the free and clotted blood present in the abdominal cavity, than any form of drainage. From my own experience, and from my knowledge of the experience of others, I may state unequivocally, that drainage in extrauterine pregnancy delays convalescence, prolongs morbidity, and raises the mortality rate.

*When to operate.*—This problem still absorbs the attention of gynecologists. My answer to this query is, operate as soon as possible after the diagnosis is established. Waiting for the symptoms of shock to subside, before rendering the life-saving surgical aid, is meddlesome therapy. Clinically it is difficult to differentiate, in many cases, between shock and hemorrhage, and is not shock in ruptured tubal pregnancy due to the bleeding, and if so why not stop it at the earliest possible moment? Shock or any of its manifestations in extrauterine pregnancy never constituted an operative contraindication in my experience, and the results justify the unswerving adherence to this principle. Morphine hypodermically from a  $\frac{1}{4}$  to  $\frac{1}{2}$  grain in

actively bleeding cases is an invaluable remedy; it slows the heart action, promotes coagulation and lessens the bleeding, thus making the unavoidable preoperative delay less hazardous. Transfusion of any kind or in any form should not be resorted to until the bleeding point is under surgical control. Hawks in a review of 824 cases of extrauterine pregnancy, pointed out, that the mortality in the cases operated upon after the subsidence of the initial shock, was 17 per cent; while in those operated upon during shock and collapse, the death rate did not exceed 8.8 per cent.

*Operative conservatism.*—This note is sounded from time to time from different medical centers. Cartozolla and Dossera advocated quite recently the milking of the gestation products from the tube and leaving the latter in place. Ramsay based his proposition of conservatism on the experience of one case in which an intrauterine gestation followed such a procedure, in a patient operated upon for a successive tubal pregnancy, and had had this only tube at that time. Borell, Fink, Fränkel, Falk, Goebel, Martin, Micholitsch, Matushima, Nuerenberger, Orthmann, and others, have preached conservatism, basing their teachings upon the fact that some cases of tubal pregnancy may go on to spontaneous healing, through the absorption of the ovum or through the conversion of the pregnancy into a mole or polypoid formation which may continue indefinitely in this state without giving rise to any untoward symptoms. No one denies the possibilities or the actual occurrence of these end-results, but they form the rare exceptions, while the majority of the tubal pregnancies go on to rupture with all its dire results. And who is clinically so astute as to be able to predict which of the two described courses an ectopic gestation will pursue? Since we have no criteria by which to foretell these eventualities, and since bleeding from a pregnant tube may go on even after the ovum has been removed or has escaped, as was shown by Fromme, and later substantiated by Aschoff, and Pankow, the conservative form of therapy should occupy an academic but not a practical place in our treatment of ectopic gestation. In this opinion share Bozemann, Frankl, Muret, Mandl, Schmidt, Sanger, Werth, and all the leading American surgeons. The only conservatism that I practice is the preservation of the corresponding ovary whenever possible.

*Prophylactic sterilization* in ectopic pregnancy is in my opinion an unwarranted procedure in the usual run of cases. The fact that the number of intrauterine gestations following ectopic pregnancy ranges from 20 to 52 per cent and that the recurrent tubal pregnancies occur in only 2.7 to 7.9 per cent, speaks against prophylactic sterilization as a routine procedure.

*Symptomatology.*—Under this heading I wish to consider only the rarer and the more recently described and rediscovered clinical phe-

nomena of ectopic gestation. Anuria occurs in some cases of ruptured extrauterine pregnancy in which the intraperitoneal bleeding is excessive. It sets in from two to twenty hours after the rupture, according to the observations of Hovart, Herzfeld, Mandelstamm, and Piskacek. That this anuria is not due to a concomitant nephritis was proved by the absence of albumin and casts, and by the negative eye findings. This urinary suppression is explained by the low blood pressure which accompanies large intraabdominal hemorrhages, hence the failure of the glomeruli to act as filters. Shoulder pains occur whenever the free blood in the peritoneal cavity finds its way to the subdiaphragmatic spaces, where it irritates the sensory branches of the phrenic, and from there it is transmitted to the shoulder area through the cervical branches of the fourth spinal nerve. The first observer who called the attention of the gynecologists to this symptom was Oehlecker of Hamburg, in 1913. Dewes, Herzfeld, Rubin, and Lafont, have also described this sign, within the past three years. This sign appears only when the quantity of blood in the abdominal cavity is excessive and is of value only after having excluded other conditions, such as cholelithiasis, liver abscess, adrenal tumors, and accumulations of gas or fluid from ruptured viscera, all of which may give rise to similar phenomena. Cullen's sign was described by its author in 1919 as follows: "The umbilicus itself is of a greenish hue. Above the navel is a faint bluish tinge, below the umbilicus the bluish appearance is more intense." Cullen's comment on this sign reads thus: "Whether it will prove to be of common occurrence or very rare, I cannot say, but we shall undoubtedly expect it only, when there is free blood in the abdomen, and shall be more likely to encounter it in thin individuals." Hellendal, Kapsinow, Novak, and Strube, have also observed this sign. Veit has also mentioned it and claimed that the discoloration of the umbilical area was due to a venous stasis in the tube wall brought about by their blocking with chorionic villi, and that this stasis extends to the hypogastric vessels. Other authorities claim that this discoloration is only the bluish shimmer reflected by the free blood through a very thin abdominal wall which is identical with the bluish hue, so familiar to the abdominal surgeon on reaching the peritoneal layer, in cases of intra-abdominal bleeding. I have thus far not had the opportunity to observe this sign, most likely due to the fact that all my patients have had abdominal adiposities varying from the enviable to the laughable, and at times reaching a pitiable degree.

#### IV. CONCLUSIONS

1. The biomechanism of ectopic pregnancy simulates the intrauterine form in the manner of ovular nidation, in the building of a

reflexa, and in the decidual response of the extrauterine connective tissue elements.

2. The main reason for the premature termination of most ectopic pregnancies is the excessive intracapsular bleeding, due to the laying open of blood vessels in the ovarian bed by the chorionic villi, which are much larger than the capillaries of the compacta in the uterus.

3. The intra- and the extratubal conditions of an organic nature are by far less responsible for the ectopic nidation of the ovum than is the disturbed peristaltic function of the tube, and the premature ripening of the placentation properties of the ovum.

4. The terminologies "unruptured tubal pregnancy" and "tubal abortion" are incorrect, for they do not express the true pathologic state. All ectopic pregnancies, even those going to term, sustain capsular ruptures of greater or lesser degrees, at some time during the gestation period. A so-called "unruptured tubal pregnancy" is in reality an "intra capsular rupture," and a "tubal abortion" is an "internal rupture" with the gestation products discharged into the tube lumen, which finally escape through the fimbriated end.

5. The point of rupture in the majority of my cases was found opposite the placentation site; this is contrary to the accepted teachings. The correctness of my observations is sustained by the following facts: (a) During the early weeks of pregnancy the chorionic villi are equipotent and they may arrode any part of the capsularis, and (b) the part of the capsularis that will yield first is the thinnest and the most stretched portion, which is usually not the placental area, for the latter always shows the greatest amount of hypertrophy and hyperplasia.

6. Uterine bleeding manifesting itself during the course of an ectopic pregnancy, indicates fetal death, and a simultaneous suspension of the inhibitory power of the corpus luteum over the endometrium, which is the only source of the uterine bleeding.

THE TREATMENT OF ECLAMPSIA WITH BLOOD SERUM FROM  
ECLAMPTICS\*  
(PRELIMINARY REPORT)

BY JOHN J. McMAHON, M.D., NEW YORK, N. Y.

I BELIEVE we will all concede that our theories as to the cause of eclampsia are not clearly defined. The treatment of eclampsia is likewise unsatisfactory, as is evident from the high mortality. For a long time I have had in mind the possibility of using blood or blood serum obtained from recovered eclamptic patients for injection into acute cases.

On November 23, 1924, a colleague at St. John's Hospital, Long Island City, had a patient who was desperately ill and seemingly in the final stage of eclamptic coma. The case seemed hopeless, and, as we happened to have in the hospital on our service an eclamptic five days postpartum, who had recovered, it seemed a very opportune time to try out the theory. From November 23, 1924, to January 7, 1926, we used this serum in ten cases.

CASE REPORTS

CASE 1, St. John's Hospital.—Mrs. S., para i, aged twenty-one years, born in U. S. Last menstruation March 3, 1924. Estimated confinement December 10, 1924. Admitted at 11:30 P.M., November 22, 1924. Temperature 103° F. Five convulsions before admission. Blood pressure 190/130. Four convulsions after admission. At 5:30 A.M., November 23, 1924, after a convulsion, she developed marked pulmonary edema, cyanosis and dilated, sluggish, divergent pupils. Patient's condition grave. Had morphine  $\frac{1}{4}$  gr. on admission; repeated once. Had hot pack and colonic irrigation. Because the fetal heart was thought to have been heard, abdominal section under oxygen was done at 8 A.M.; stillbirth, female. B. P., 5 A.M., 152/100, at noon 94/64, and when seen by me at 3 P.M., 84/80. Patient was getting oxygen with little apparent relief. Had had adrenalin minims 15, caffeine 7 gr. and atropine  $\frac{1}{150}$ . Pulse absent at radials. After blood typing at 3:45 P.M. she was given by direct transfusion 100 c.c. of blood from our recovered eclamptic. In this case the result seemed almost miraculous. The pulmonary edema seemed to begin to clear immediately and in a few hours the whole picture changed. In two hours pulse and heart had improved. Patient was conscious and took small amounts of water and nourishment. The edema had entirely disappeared within three hours. Temperature dropped in twelve hours to 98.6°.

Urinalysis: sp. gr. 1030, alkaline, heavy trace of albumin, hyaline casts.

Blood chemistry: Urea N, 13; creatinine, 1.6. Her blood and the donor's blood were Type II. On the fourth day a rise in temperature was caused by infection of the abdominal wound. Discharged on December 20, 1924.

The history of the donor was as follows: Mrs. J. S., aged twenty-four years, para

\*Read at a meeting of the Medical Society of the County of New York, February 24, 1926.

i, born in U. S. admitted November 19, 1924, in convulsions. B. P. 150. Version and extraction, stillbirth.

The urine contained a large amount of albumin with hyaline casts. The blood showed urea N, 12.2; creatinine, 2.1; and sugar, 76. On November, 24, 1924, on the fifth day, was in very good condition when blood was taken.

Encouraged by the result in this case we decided to secure serum from our next recovered eelamptic for future use. We prepared the serum in the following manner. At St. John's Hospital the blood was received in 500 c.c. Erlenmeyer flasks and kept for two hours at room temperature in slanted position, then overnight at ice box temperature. The serum was pipetted into 50 c.c. flasks and 0.25 per cent tricresol, dissolved in about 5 c.c. of saline, added and the flask sealed. At the Misericordia Hospital it was prepared somewhat in the same manner. The blood was turned into a sterile vessel and allowed to clot, the serum decanted off and 1 per cent of phenol in normal salt solution added, equal parts of the serum to the saline, and stirred slowly. It was then sealed and kept in the ice box. A Wassermann and blood typing was also done.

**CASE 2**, Misericordia Hospital.—January 7, 1925. Mrs. K., para i, aged twenty-two years, born in U. S. Last menstruation April 18, 1924. Estimated confinement January 30, 1925. December 12, 1924, when last seen by physician urine was clear, no albumin. B. P. 115. January 7 when admitted to Misericordia, B. P. was 160/100 and she had had ten convulsions from 1 P.M. until 11:45 P.M. At midnight she was given 45 c.c. of serum from Type III recovered eelamptic ten days' postpartum. The serum was injected into the buttocks. The patient had one convolution just as she received the serum and one convolution one-half hour later. She went into labor and the head came on the perineum at 10 A.M. and was lifted off with forceps. Three loops of cord were about the neck. Baby could not be resuscitated. Fetal heart was heard at 2 A.M.

This urine boiled solid, contained many hyaline and granular casts. In thirty-six hours after injection of serum urine was practically clear, the very faintest trace of albumin being seen.

The urea N was 23; creatine, 2.2. Discharged eleventh day postpartum.

**CASE 3**, St. John's Hospital.—March 25, 1925. Mrs. I., para i, aged twenty-two years, born in U. S. Four convulsions before admission. Delivered of living twins. Temperature 101° F. on admission. Had five convulsions after delivery, and received 60 c.c. of serum into the gluteal region seven hours later. Had one slight convolution twenty minutes after the injection. Had only a slight trace of albumin in her urine with no casts. The blood chemistry showed: Urea N, 12; creatinine, 1.9, and sugar, 80. She was discharged on the eleventh day postpartum with a hemoglobin of 45 per cent. Her blood and the donor's blood were Type II.

**CASE 4**, St. John's Hospital.—April 6, 1925. Mrs. A., para i, aged nineteen years. Admitted at 4 A.M. in convulsion with temperature of 105°. B. P. 160/120. Had seven or eight convulsions before admission and three after reaching the ward. Had marked pulmonary edema and was in grave condition at 1:30 P.M., when she was given 58 c.c. of serum into the gluteal region. Four hours later went into labor and was delivered of a stillborn child. Twelve hours after the injection of the serum the edema had disappeared. She had two convulsions after injection of serum.

The urine showed a heavy trace of albumin and hyaline and granular casts. The hemoglobin was 70 per cent. This urine on the second day was clear. Her blood was of Type II. Discharged on the tenth day postpartum.

CASE 5, St. John's Hospital.—May 10, 1925. Mrs. G., para iii, aged thirty-seven years, born in Russia. In October, 1924, had gall bladder drained for gallstones. Admitted as preeclamptic. Urine had been clear from January 12, 1925, up to May 3, 1925, and blood pressure had been 130/100 during that period. On May 3 showed a large amount of albumin and casts and B. P. rose to 180/110. Marked edema of the face and extremities. Was admitted with a severe headache. Put to bed and given the usual treatment. In ten hours she had convulsions, six in all. Delivered spontaneously, stillbirth. Marked cyanosis and pulmonary edema. Note on the chart states she expectorated large amount of foul-smelling mucus. Before delivery she was bled 500 c.c. and was in a desperate condition when given 50 c.c. of serum on May 11 at 10 A.M. She died on May 13. For twenty-four hours she seemed to be improved, had no convulsions, and on the advice of a medical consultant was given 500 c.c. of saline, intravenously. Blood was of Type II and she was given serum of Type II. This serum was inactivated. This was the only serum that we gave which had been inactivated. The records are incomplete on her blood.

CASE 6, St. John's Hospital.—May 19, 1925. Mrs. McL., para ii, aged twenty-two years, born in U. S. Admitted in convulsion at 11 P.M. B. P. 150/90. We tested this patient for a reaction by intradermal and subcutaneous injection before giving her the serum, and there was no reaction. She was given 40 c.c. of Type II serum into the buttocks after third convulsion. She was also of Type II. Temperature 100°.

The urine contained a heavy trace of albumin, sp. gr. 1028, and granular casts. Blood chemistry showed: urea N, 13; uric acid, 5.7; creatinine, 1.4; sugar, 50; and N. P. N., 25; Wassermann negative.

Made a very prompt recovery. Had no convulsions after the injection and was discharged on the ninth day after admission, as she insisted that she felt perfectly well and still felt fetal movements. We were unable to hear the fetal heart. Two weeks later she had a spontaneous delivery at home; stillbirth. She made an uneventful postpartum recovery at home.

CASE 7.—This case occurred at Lincoln Hospital, on the service of Dr. E. Davin, through whose courtesy I am reporting it. June 7, 1925. Para i, aged twenty-one years, born in U. S. Last menstruation September 10, 1924. Estimated confinement June 17, 1925. At the sixth month had pyelitis, which was supposedly cured. Urine on admission was clear, very few pus cells. B. P. 120/70. Note made after examination by neurologist,—“Vomiting and slight headache. Pupils dilated and reacted to light and accommodation. Having semiunconscious periods lasting about a moment. Acts peculiar, is irrational. Cranial nerves, arms and legs normal. Reflexes normal. Attacks resemble petit mal. Mild psychosis of pregnancy rather than hysteria.”

On June 10 had a severe convulsion lasting several minutes. Pulse rapid. Unconscious. Had seven or eight severe convulsions during the day. In spite of negative urine, blood pressure and blood chemistry, a diagnosis of eclampsia was made. A spinal tapping was done, and 30 c.c. of clear fluid obtained under markedly increased pressure. Phlebotomy of 100 c.c. at 4 P.M., and at my suggestion at 4:10 P.M. 60 c.c. of serum was given intravenously. At 5:10 P.M., one hour later, 100 c.c. of serum was given intravenously. Patient had one convulsion ten minutes after serum. No further convulsions. At the time of convulsion her temperature was

104°, pulse 140. Three hours after the serum was injected, temperature 104°. Then began to drop and in twelve hours reached 99°. Patient's condition on June 11 seemed weak; resting comfortably, perspiring freely. Vomited some green fluid twice during the day. On June 12 very much improved. Temperature 98°. Mental condition normal. On June 13, maceerated stillbirth. Condition of patient very good. Placenta was adherent and retained. Manual extraction. Patient put to bed in very good condition. Thirty-six hours later patient had a severe chill, rise in temperature to 103° and five days later died of sepsis, as shown by a positive blood culture showing Streptococcus viridans and hemolyticus.

The blood chemistry showed: Urea N, 13.9; creatinine, 1.33. Blood was of Type IV. She received serum from Type II.

CASE 8, St. John's Hospital.—July 11, 1925. Mrs. E. B., para i, aged eighteen years, born in U. S. Spontaneous delivery of living child at 5 A.M. at her home. Convulsion at 7:45 and three other convulsions before admission to the hospital. She had eleven convulsions after admission. Temperature was 106°. She was given 58 c.c. of serum in the gluteal region after thirteen convulsions and had two slight convulsions within one hour after the serum had been injected.

The urine showed a heavy trace of albumin and granular casts. The blood chemistry showed: urea N, 13.2; sugar, 110; creatinine, 1.2. Discharged July 27, cured, sixteen days after admission. Blood of Type II.

CASE 9, Misericordia Hospital.—June 24, 1925. Mrs. O. B., para i, aged twenty three years, born in U. S. Spontaneous delivery. Eleven hours later convulsions, thirteen in all. Was given 90 c.c. of serum intravenously after seven convulsions. Had six convulsions after the serum. This patient was seen in consultation when in convulsion. Discharged August 7, thirteen days postpartum.

The urine showed large amount of albumin and granular casts. Just before her convulsions she had marked edema of the extremities. This patient was Type I and received serum from Type II.

CASE 10, Misericordia Hospital.—Para i, aged seventeen years, born in U. S. Three convulsions before and thirty after delivery. Temperature 104° before serum was injected and 99° twenty-four hours later. She was given 50 c.c. of serum, about one-half of it intravenously and the remainder in the muscle of the back. Was delivered of a full-term living baby. B. P. 155/119.

The urine showed large amount of albumin, granular and hyaline casts. Twenty four hours after serum no casts in the urine and moderate amount of albumin. The blood chemistry showed: urea N, 13; creatinine, 1.5; and sugar, 90.

No convulsions after serum was injected. The baby had many convulsions for two days similar to those of the mother and died on the sixth day.

#### SUMMARY

Ten cases: eight primipara, two multipara. Eight antepartum and two postpartum eclampties.

Ages: One, seventeen years; eight under twenty-three years, and one thirty-seven years old.

Five living children and six stillbirths. Serum had been inactivated in one case. Three received the serum intravenously with no reaction, seemingly prompt improvement. All others received the serum intramuscularly. Smallest dose, 40 c.c. of serum; largest dose, 160 c.c. Highest temperature, 106°; lowest temperature, 100°; all patients had

some fever. Convulsions varied from four to thirty. All serum was given from Type II or IV.

One had six convulsions after serum; three had two convulsions after serum; two had one convolution after serum; and four had no convulsions after serum.

Albumin seemed to clear very rapidly in four cases after the injection of serum.

I am reporting these cases because we were impressed by the unusually prompt and unexpectedly favorable reactions which followed the use of the serum in the majority of these cases. Two of these patients were beyond question desperately ill and apparently hopeless at the time the serum was used. We are unable to offer any satisfactory explanation for these results, but we feel and we hope that they may open up a line of experimental and clinical investigation which may bring forth something of practical value in the therapy of this disease.

I am indebted to Dr. Carl Boettiger, Director of Laboratory, St. John's Hospital, and Dr. R. Schleusner, Misericordia Hospital, for their assistance in the preparation of the serum.

148 WEST EIGHTY-EIGHTH STREET.

## VARICOCELE OF THE BROAD LIGAMENT\*

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IN MUCH of the discussion of varicocele of the broad ligament, the old classification of two types is considered: (a) primary or idiopathic, and (b) secondary. The primary or idiopathic type is a true dilatation of the veins and not associated with any other lesions, disturbances, or growths in the pelvis. The secondary type is always concomitant with pelvic abnormalities or diseases. The incidence of type one is so rare that gynecologists of large experience covering a period of many years have not seen a single case.

As the pathogeny of the idiopathic type is disputed, it is evident that many are accepting a broad interpretation of the meaning of the word "idiopathic" and are holding to the conception of primary pelvic varix as due to congenital or developmental defects, hence its rarity. And further, where the pathognomy of varix is dependent upon lacerations, the incidence of pregnancies, displacements, and the many predisposing factors that retard the pelvic circulation, this varix is a concomitant or sequela and should be classified as type two

\*Read before the Surgical Section of the Academy of Medicine of Toledo and Lucas County.

or secondary, but many writers still consider it as belonging to type one or idiopathic.

These idiopathic cases should be classed as pure varicocele and are to be differentiated from those where there are lesions of the adnexae and uterus, which should be classified as type two.

The occurrence of type two, however, is exceedingly common in the aggregate, and if we exclude the varix due to large growths, it still remains a clinical picture of much frequency.

A perusal of case histories reported in the literature will classify many of them as representatives of the secondary type of varix. During nearly thirty-five years of surgical work I have not had a single case of the idiopathic type. Many cases may seem so at first, but subjecting these border line ones to a final critical analysis, they fall under the heading of type two.

To elaborate this statement the following case report is of interest.

In 1902 I was called to a small town to perform a hysterectomy for a supposed cancer of the fundus. The patient, a farmer's wife, mother of a large family, age sixty, was having excessive and repeated uterine hemorrhages. Examination was negative. Pelvic organs apparently normal following the climacteric. On opening the abdomen, marked varices of both broad ligaments involving not only the ovarian but the uterine venous plexus, were noted. No other abnormalities. Panhysterectomy was performed. Patient recovered. Microscopic examination showed no malignancy.

This varix was secondary, a concomitant of many pregnancies, of various infectious diseases, and of excessive manual work, manifesting itself late owing to atrophy and circulatory changes incident to the climacteric, and now classed in the group of organic lesions of permanent dilatation.

Fothergill insists on making clear and differentiating these types and classifies varices as secondary, not only those associated with fibroids and other newgrowths and with cases of old pelvic infection, but also those where there is marked retroversion.

Therefore, if writers adhere to such differentiation, it necessarily must follow that type one, or pure varix of the broad ligament, is exceedingly rare.

The recent modern classification of this disease, due to the research work and investigations of Castano, Hertzler, and Emge, has clarified many disputed points in their entirety, not only as to pathogenesis, sequelae, and complications, but also to the proper surgical procedure.

Castano's investigations led him to assert that pure varix is due to primary organic changes in the vessel walls, the resultant of infection, principally syphilis. Hertzler remarks (1913) that in simple passive hyperemia the vessels may contract and disappear when focal lesions which called them forth subside.

These hyperemias fall into several classes. When dilatation persists, the vessels lose their power to contract and remain permanently dilated regardless of the initial lesion. The incidence of varix is more prone where general laxity of the fibrous tissue and the vessels in particular exists.

Emge (1925) continues the classification of Hertzler and others of the tem-

porary or nonsurgical type, and the permanent or surgical type. The latter is subdivided into two groups: the first, venous dilatation due to disturbed support or control of vessels without any anatomic changes in the vessel wall; the second group includes those in which anatomic changes have taken place, usually due to inflammatory lesions. He further states that "true varicoceles are practically confined to the latter division." In the first group, functional changes precede the organic changes, while in the second group organic lesions form the starting point. The first group is more common and responds to constructive surgery. The second is rarely seen and demands resection of the affected vessels.

In a recent report of 24 cases he classifies 23 as belonging in the first group and 1 in the second.

It is the purpose of this paper to refresh your minds concerning the significant diagnostic symptoms and the etiology; to present the surgical methods employed upon the varices, and above all to stress conservatism during genital life which is in keeping with our knowledge of the complications of varix and of the value of the endocrine glands.

Richet and DeValz (1860) described a case of primary uterine varicocele unrelated to any pelvic lesion.

Dudley (1888) reported four cases treated surgically, commenting on the influence of varix on the ovary and the histologic study of the excised veins.

In 1891 Petit gave an anatomic and histologic report on the ovary and varices of a sclerotic uterus removed by Pozzi.

From then on the literature is that of reported isolated cases, studies in diagnosis, pathology, symptoms, and treatment.

Castano, in 1913, began to study pelvic varicocele, since which time he has written much of great value, and advocated the "Argentine method" for radical cure.

Emge, in 1921 and 1925, reported his observations of 35 cases in his first monograph and 24 in his last, with much valuable data. He concludes that varicose veins are due in the vast majority of cases to damage of the fibroelastic suspensory; conservative measures are usually sufficient; shortening the uterosacral and associated ligaments by special suturing and aided by round ligament transplantation; resection of veins is unnecessary unless there are varicosities due to inflammatory lesions.

In six hundred and fifty laparotomies Cotte, 1923, found seven typical cases presenting diagnostic symptoms, but with retroversion of the uterus. Ligation and excision of veins in the lomboovarian ligament with correction of retroversion resulted in cures.

#### ETIOPATHOGENESIS

Richelot described a congestive condition of the female pelvis at puberty, with well-marked clinical symptoms, that leads to a state of diffuse sclerosis and which might form the beginning of the pathologic history of pelvic varicocele.

Castano analyzed the living conditions of his patients and found unsuitable work during puberty, hard labor without adequate alimentation or proper habits, were predisposing factors, conducive to congestion, but would not cause the condition. He found these changes were the result of infection, acute rheumatism, influenza, tuberculosis, etc., but the main factor was hereditary or acquired syph-

ilis; that these specific poisons produce a venous and arterial dystrophy or sclerosis. This sclerotic tissue encircles the vein, involves the adjacent nerves and causes the neuritis of varicocele.

Richel states the venous plexus is poorly supported in the subperitoneal cellular tissue and their walls cannot withstand the blood pressure.

Auvray suggests some congenital anomaly of venous development.

Chalier and Dunet (1920) believe lesions of the ovary are a common association of and probably the primary cause of varix. In reporting a case of essential tubo-ovarian varicocele in a woman of twenty, they assert that Camuset was able to find only seven authentic case reports in the literature. In their case the uterus and right side were normal, but an enormous development of the left uteroovarian veins formed a vascular tumor. The left ovary was small and scleroectic, and showed extensive cystic degeneration of graafian follicles, marked follicular atresia and hyperplasia of the lutein cells. They theorize that the ovary plays an important part in the pathogenesis and that the internal secretion of the ovary is the most important factor in the vascularization of the entire genital tract. In such an ovary the number of cells of internal secretion is increased and hyperfunction results.

Darnall (1917) reports thirty cases. It most often prevails in patients who have borne children, and is especially true if the perineal supports have been impaired. He believes that venous stasis is the cause of the pathologic states found in the ovary, rather than a result.

Kelsall (1921) believes varix is more frequent than supposed and assigns among other causes subinvolution of the uterus and ovarian vessels with persistence of pelvic engorgement, due to laceration of the pelvic floor; with the accompanying malposition of the uterus, torsion of the vessels is produced and the consequent obstruction to the free flow of blood causes venous dilatation.

Emge (1925), in reviewing the anatomic studies of Blaisdell on the basal ligaments of the pelvis and the perivascular tissue of Cameron, which are functionally inseparable and which maintain a variable degree of traction which in turn produce a controlling pressure on the blood vessel they ensheathe, believes they not only constitute a large part of the pelvic support, but are indispensable in the control of normal venous and lymphatic pelvic circulation.

#### SYMPTOMS

The subjective manifestations of varix are varied and abundant, ranging from hysteria to melancholia. The most common complaint is continuous pelvic pain with rectal and vesical tenesmus, aggravated previous to menses and alleviated during flow. The menstrual flow is abundant and of the menorrhagia type, often merging into metrorrhagia.

Following menses, leucorrhea of the hydrorrhoea type develops; congestion of the venous plexus adjacent to the clitoris produces a "permanent voluptuous sensation" at the least stimulation, not gratified, owing to dyspareunia.

The objective signs are but few and are usually of a negative character. They may be local and general.

In the local manifestations varix may be associated with a large uterus in retroflexion with edematous ovaries, painful rugosities in

the vaginal wall, which may be hot, turgid, and edematous. The varicosities may be palpated in the upright position.

The general physical signs are those of endocrine dysfunction. The congestive hypothyroid type described by Hertoghe, Levi, and Rothschild (varix of legs and labia) and of hyperovarianism and hypothyroidism.

#### SURGICAL TREATMENT

To survey and interpret a few anatomic facts in order to apply proper curative surgical technic it will be *apropos* to mention briefly the pelvic venous system.

The vaginal, hemorrhoidal, vesical, and uterine plexus drain into the inferior hypogastric veins and follow their corresponding arteries, surrounded by a dense connective tissue mixed with muscle fiber. With certain few exceptions, venous overdistention and permanent dilatation are safeguarded by this dense perivascular tissue.

The pampiniform plexus empties through the ovarian veins into the vena cava on the right side and the renal vein at right angle on the left. They are long and tortuous, with numerous branches and are practically devoid of connective tissue and muscle support. Such anatomic development renders them susceptible to temporary and permanent dilatation; the left plexus more so, owing to the absence of a valve in the vein.

The surgical technic adopted should be guided by the pathology and type of varix presented.

Emge sums up his cases thus: damage of the fibroelastic suspensoryum produces varix in the majority of cases, and proper shortening of the round and sacrouterine ligaments is productive of success. Resection of veins is indicated only where anatomic changes in the vessel wall have taken place.

In the past, I have been splitting the broad ligament posterior to the round ligament, exposing the varices, ligating with excision, and closure of the peritoneum.

This was abandoned, owing to incompleteness, distortion of tube, and sometimes hematoma of the broad ligament. In several instances it was necessary to remove the healthy tube, due to the above complications, since which time mere double ligation of vessels with linen, through the broad ligament, has been practiced with restoration of pelvic supports.

As before stated Cotte (1923) ligated and excised the veins in the lumboovarian ligament; Castano devised and published (1925) what he designates the "Argentine method," which appeals to our anatomico-surgical sense for positive results. It is simple and easy, and overcomes the mechanical cause of varicocele. He splits the peritoneum

on the ilioovarian ligament, dissects the uteroovarian venous trunk which is double, isolates, and cuts between ligatures; the peritoneum is closed with catgut.

#### COMMENTS

I maintain that, in our modern classification of pelvic varicocele, we should retain the idiopathic type or pure varicocele. As before stated, Camuset found but seven authentic cases reported in the literature. In deference to these fortunate writers and in justice to their memories as well as to clinical and surgical significance of this type, though rare, it should be a part of our classification. It clarifies this subject, it will end further disputes, and aids in the placement of varix in its proper type or group.

Castano has stated that infection plays an all important part in the causation of organic lesions of the pelvic veins from simple hyperemia to permanent organic dilatation and finds that syphilis is predominant. In our earlier cases this etiologic factor may have been present, but since our routine Wassermanns, I fail to find it a predominating factor. And when present, it has been a potent factor in the development of disturbing sequelae postoperative.

The disastrous effects of the streptococcus on the circulatory system are common clinical manifestations and I have noted, in the past few years, more cases of pelvic varix than ordinarily since the visitation of the epidemic of influenza. Permanent and satisfactory results are obtained in the pelvis, as well as other organs of the body, only when these foci of infection are completely eradicated.

The personal and clinical history of the patient is of the utmost importance in the determination of the surgical technic to be adopted. I have made it a rule that, in the presence of general infection and especially associated with menorrhagia, the shortening of ligaments and repair are supplemental to ligation or excision of veins. And further in this connection that during genital life no associated ovarian cysts that were present warranted ablation, our clinical experience coinciding with Darnall's statement that venous stasis is the cause of the pathologic states found in the ovary, rather than a result.

The preceding methods represent in the vast majority of pelvic varices the surgical technic to be adopted. There are, however, certain types of cases that warrant and need radical procedures other than those above advocated. In the first type or idiopathic, the mode of procedure should be dictated by the size of the mass, to assure success.

While I hesitate to be dictatorial, surgical judgment would indicate something more than suspension and ligation and excision in the iliac lumbar ligament.

Reasoning from analogous varix manifestations in the extremities, when resection has taken place at different levels, the occasional sequela of thrombophlebitis from effects of tubercle bacillus, spirocheta, and streptococcus, often necessitates the removal of the entire vein.

So here mere resection in the ovarian ligament could by the complication of thrombosis, infection of broad ligament veins, etc., produce an affection equally as disturbing as that for which the procedure was employed, and necessitate further laparotomy for complete excision.

As before stated, in my experience, it was necessary through accidental complications to remove in several cases the broad ligament as well as the tube, but conserving the ovary, with eminently satisfactory results, so it seems that surgical principles would dictate complete excision of the protuberant mass of veins, and in so doing the broad ligament and tube should by their close intimacy be removed *en bloc*.

In the advanced climaacteric varieties there are two types that are sometimes associated with pelvic varicocele.

The first of these is represented by permanent dilatation of veins, with laxity of supports, malpositions, and complete procidentia. Where conservation of the uterus is desirable in this variety, and where no organic lesions of the veins are present, the surgical technic in no wise should differ from the conservative methods as adopted and advanced for those in genital life.

The second variety is represented by atrophy and sclerosis of tissues, with contracture of ligaments and fixity of uterus, and associated permanent organic dilatation, of not only the tuboovarian veins, but also the uterine plexus. Here, too, are often found the rectal, vesical, labial dilatations with varix of the extremities.

I have had occasion to operate upon many of these patients who presented the pathologic picture as stated, and whose clinical picture of pelvic pain and excessive hemorrhage was uniformly present.

While I am open to conviction, I confess a timidity and have a lack of assurance as to the end-results in merely resecting the ovarian veins for this condition, and until such time as statistics will disprove this radical operation, I shall still advocate panhysterectomy for the climaacteric variety.

## THE PREOPERATIVE RESPONSIBILITIES OF THE GYNECOLOGIST\*

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SINCE most pelvic operations are elective and but few emergent, the gynecologist usually has ample time for thorough preoperative study and preparation of his patients. Yet it must be conceded that not infrequently after operation the patient is disappointed by the persistence of symptoms or the surgeon distressed by an unexpected death. The prevention of these unfortunate eventualities is a problem, worthy of serious consideration. Expert anesthesia, asepsis, and the easily acquired technic have made pelvic surgery so safe that postoperative recovery can no longer be accepted as the sole criterion of success. The patient submits to operation because she is led to believe that her symptoms cannot be relieved otherwise, and that the repair of anatomic injuries or removal of diseased tissue will cure her ailments. How incumbent it becomes upon the gynecologist, then, not only to detect pathologic changes, but also to correlate cause and effect correctly, so that the purposes of the operation may be fulfilled in every respect. Even with operators of intellectual honesty and highly developed diagnostic acumen, unsatisfactory results and surgical disasters follow pelvic operations sufficiently often to justify a critical survey of the factors concerned in their causation.

The gynecologic examination of the patient is a simple matter; the examination of the gynecologic patient is a complicated procedure. The former can be accomplished in a few minutes; the latter takes time, and involves the exercise of all our diagnostic resources. The tendency to forget that the exciting cause of symptoms may be either remote or local is so great that, in the presence of frank pelvic pathology, a coexisting lesion elsewhere may not even be suspected or sought. For example, alterations in the menstrual function are not infrequently manifestations of constitutional disease, secondary anemia, neuroses, or the inherent peculiarities of the patient, as well as of endocrine imbalance, uterine neoplasms, and adnexal disease. Leucorrhea, particularly in virgins, is as likely to arise from impaired physiologic processes as from pathologic pelvic conditions. A vaginal discharge is frequently associated with anemia, and promptly cured with iron and arsenic. In several cases of leucorrhea occurring in adolescent girls, radiography of the chest disclosed the presence of

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an incipient pulmonary phthisis. The futility of local or operative treatment under such circumstances is obvious. Sacral backache may be due to retrodisplacements of the uterus, but it may also be an expression of focal infection, an overloaded colon tugging on its mesentery, sacroiliac strain, posterior parametritis, and numerous other etiologic abnormalities. I confess to personal embarrassment in two instances in which this type of backache continued after plastic and round ligament operations, and in which it was promptly relieved by subsequent tonsillectomy. I operated upon another patient with adherent retroflexed uterus, and was chagrined afterward to find that the backache persisted until the plantar arches were supported. Pain in one of the lower abdominal quadrants sometimes serves as the pretext for the removal of an ovary or the appendix, when the real cause of the annoyance lies in the urinary tract. In one case of this character, seen about ten years ago, the patient had been subjected to a left oophorectomy and tubal resection by another operator two years before I saw her. Since the inguinal pain had recurred, I made the mistake of operating upon her again, removing a hydrosalpinx in the stump of the left tube, and the right ovary, which had become cystic. It soon became evident that the second operation had also failed of its object, and that the exciting cause of the pain must be searched for elsewhere. A renal function test, ureteral catheterization, and pyelography demonstrated a pronounced stricture of the left ureter, which was easily cured by dilatation. I have never done an elective gynecologic operation since then without preliminary cystoscopy and an indigocarmine renal function test. In a careful analysis of 600 consecutive private case histories, it was surprising to find that 119, or 20 per cent, of gynecologic patients had some definite lesion of the urinary tract or symptoms referable to it.

From the foregoing premises, the following inferences seem justified: a liberal amount of time should be allotted to new patients; history-taking should not be delegated to office assistants; a complete physical inventory is essential; cystoscopy is an indispensable aid to the gynecologist, and a renal function test should be done before every elective operation. The further one advances in the practice of his specialty, the more serviceable are found the fundamental principles of diagnosis.

Some years ago Sir D'Arcy Power formulated the following aphorisms in describing the developmental stages in a surgeon's career: "In the first, he loses his fear of hemorrhage; in the second, he ceases to multiply operations; in the third, he acquires the moral courage to stop in the middle of an operation when he finds the condition inoperable. There is a final stage which he never acquires with the present

span of life, the ability to gauge correctly the vital resistance of the patient; yet on this depends the success of every operation." At the present time, however, we seem to be approaching the elusive fourth stage, by invoking the aid of modern laboratory procedures. Most surgical catastrophes are the result of serious constitutional or metabolic impairment, and while it is true that some patients may recover in spite of such derangements, others will surely die of them if they are not discovered and corrected. The constantly broadening field of biologic chemistry has furnished so much enlightening information that, with painstaking preoperative investigation, our prognostic facilities are tremendously enhanced. It is therefore better to devote the necessary attention to these details than to rue the oversight of them after the grave has been filled. I admit that routine laboratory examinations have been overpopularized, and that occasionally there is danger of a laboratory report superseding clinical judgment, but this is an extreme to which I have no reference. It is quite possible to become proficient in the science of medicine and still practice the art.

No general anesthetic should be administered, except in emergency cases, without an examination of the heart, and if there is marked evidence of cardiac functional disturbance, an electrocardiogram and renal function test should be done. Many operative cardiac deaths are renal deaths. Those patients who show lengthening of conduction time should be digitalized. Cases of aortic lesions and mitral stenosis are always hazardous. Good compensation of all valvular leaks is of paramount importance, and if time is necessary to secure it, time should be taken. A compromised myocardium is often the unrecognized cause of death; unrecognized because the patient does not die of cardiac failure but of embolism or pulmonary complications. In the field of obstetrics, a patient with mitral stenosis may begin her pregnancy with apparently good compensation, and subsequently develop cardiac asthma, bronchitis, or dangerous decompensation. As the intraabdominal pressure increases slowly, the symptoms progress insidiously, are easily recognized, and appropriate therapeutic measures can be instituted before the patient succumbs. On the other hand, in operative work the complications must be anticipated; the cardiac reserve fails rapidly and there is usually insufficient time to apply corrective measures before the patient expires. The simplified technic of infiltration, parasaeral, and spinal anesthesia have done much to diminish the postoperative morbidity and mortality in patients with crippled hearts.

Arterial hypertension is nearly always associated with subnormal renal function. Blood pressure readings should be taken invariably, and the pulse pressure regarded as particularly significant. Patients

should be educated to submit twenty-four-hour and not casual specimens of urine for examination. If the daily renal excretion of urea is less than 300 grains, blood retention of nitrogenous waste products may be suspected. Indulgence in routine determination of the chemical elements of the blood places an unnecessary burden upon the laboratory. The patients upon whom such tests should be done are those over fifty years of age, those with hypertension, with poor renal function, with nephritis or diabetes, and those confronted with a formidable operation. Although chromocystoscopy is preferable for the diagnosis of urinary lesions other than nephritis, the phenol-sulphonephthalein test is a better indicator of the metabolic processes as represented by the kidneys. Abnormal quantities of urea nitrogen, uric acid, or creatinine in the blood should be reduced before any elective pelvic operation is undertaken. A salt free diet, with restricted protein ingestion, stimulation of the emunctories, absolute rest, etc., will do much to convert a poor risk into a good one.

Acidosis has been recognized as an entity and as a grave incident in operative cases for a long time. While it may be associated with hyperglycemia, it may also exist independently of diabetes. Not only is it necessary to detect its presence before operation, but also to fortify the patient against its advent afterward. This explains the practice of prescribing alkalis before operation and the inclusion of alkalis and glucose in postoperative treatment indiscriminately. Recently, however, the frequent occurrence and seriousness of alkalosis as a complicating factor has become appreciated, and this challenges the wisdom of such routine therapy. Acetone and diacetic acid in the urine, usually regarded as suggestive of acidosis, have been observed in the presence of alkalosis. I have also noted a high urea nitrogen of the blood concurrently with a greatly increased  $\text{CO}_2$  combining power. Distinction between acidosis and alkalosis is imperative, as the treatment of one exaggerates the other. The determination of the hydrogen-ion concentration of the blood and the  $\text{CO}_2$  combining power of the blood plasma are of immense practical value in differentiating the two. In fact, I believe that postoperative treatment can be regulated more intelligently with a knowledge of the  $\text{CO}_2$  combining power than with the estimation of any other single blood component. The essential cause of acidosis is usually an insufficient utilization of carbohydrate, because of an inadequate supply of the carbohydrates themselves or because of the inability of the body to oxidize them, so that a glucose solution given intravenously will soon compensate for the deficiency. The glucose has considerable value as a diuretic, counteracts the endogenous destruction of body proteins, and aids materially in maintaining renal function. Bi-car-

bonate of soda or potassium acetate may be added to advantage. In alkalosis, the remedial measures consist of hydrochloric acid and chlorides.

I would utter a word of caution against the use of radium in the pelvis of any patient with a goiter and an increased metabolic rate. Such a patient, with a rate of plus 26, was recently referred to me for treatment of a cervical carcinoma. An application of 2000 milligram hours was promptly followed by an intense thyrotoxicosis and death in forty-eight hours. Reexamination of the blood after twenty-four hours showed an insignificant increase of the urea nitrogen from 11.9 to 14, and of the  $\text{CO}_2$  combining power from 56 to 60. The systolic blood pressure, however, rose from 150 to 208. The clinical picture was that of a patient with a toxic goiter who had been given thyroxin. While these untoward effects cannot be explained, I cannot help but feel that this unfortunate occurrence was due to something more than coincidence.

Women with a pronounced anemia are universally recognized as risky candidates for operation and are transfused beforehand. I would add my voice to that of Ward and others, in a plea for the preoperative transfusion of those with lesser degrees of anemia, especially those with impaired physiologic functions, to insure a generous supply of oxygen to all the tissues. Patients with large bleeding fibroid tumors can be treated with just enough deep x-ray therapy to control the hemorrhage, and then transfused, before hysterectomy. It is unwise to transfuse the patient first, since the irradiation has a destructive effect upon the newly introduced leukocytes, particularly the lymphocytes. On the other hand, more benefit will be derived from the transfusion if the blood leak has already been stopped. Immediate operation is then no longer urgent, and additional time may be taken to reinforce the patient's vitality in other ways.

Several cases of acute pyelitis developing during the second week of an apparently smooth convalescence have impressed upon me the advisability of giving patients who show indianuria a series of colonic irrigations before operation. The oral administration of *Bacillus acidophilus* cultures also seems to help in the control of the toxic intestinal emanations, from which the pyelitis probably originates. Hexylresorecinol in full doses protects the upper urinary tract from bacterial invasion, and is a useful prophylactic agent in these cases.

The time at my disposal does not permit of the consideration of other important details that influence operative success. Neither has it been possible for me to present the biochemical aspects of the subject in a technical manner. As a clinician, I have learned to value and

profit by the information to be secured from the laboratory, not at the expense of surgical judgment, but correlating the one with the other. In emergency cases, the gynecologist must try to save life; in elective cases, he assumes the responsibility of relieving symptoms and conserving life, and must exercise eternal vigilance that life is not jeopardized.

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(*For discussion, see page 286.*)

## A SUGGESTION FOR DRAINAGE IN CESAREAN SECTION

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RECENTLY, I had an opportunity to assist in two cases of cesarean section where forceps delivery had been attempted and which were presumably infected. An infraumbilical incision was made, the uterus opened in its lower segment and closed in three layers. A cigarette drain was inserted into the pelvic cavity and the patients made very satisfactory recoveries. Both women were in extremely precarious conditions, and the blood and time saved by employing this technie made us feel that these elements were important factors in the successful outcome.

In transperitoneal section venous hemorrhage may at times prove copious and troublesome. In separating the visceal peritoneal flaps the peritoneum is undoubtedly injured, and its resistance is thereby lowered. In addition, a large raw surface teeming with lymphatics is opened to possible invasion by pathogenic germs, their toxins, or both. The majority of patients in whom transperitoneal sections are performed are usually those who have been in labor for a long time and are presumably infected. In patients of this class any technie which will save time in the performance of the operation and will conserve the patient's blood and will also provide a walled-off passage for the drainage of infected products, should prove valuable.

Drainage in connection with cesarean sections appealed to me and I have modified it for the purpose of increasing the benefits to be derived therefrom. It is believed that the initial spill does not contain the organisms responsible for peritonitis, but that peritonitis, when it does occur, is caused by pathogenic germs which invade the uterus about the fifth day and reach the peritoneum by migrating through the uterine suture lines. This latter view and the well-known facts pertaining to adhesions in the peritoneal cavity, led me to attempt the technie that I shall describe in this preliminary report. Concerning peritoneal adhesions I can best quote from Rost's book on *Pathological Physiology* (translated by Reisman): "The foreign body is such an effective stimulus to the formation of adhesions that a pus

focus will be walled off from the remainder of the abdominal cavity in twelve hours (Voleker). Indeed even such a mild irritant as a rubber or glass tube stimulates the formation of enough adhesions to prevent the evacuation of pus except from the sinus through which the drain passes."

*Technic.*—The patient is catheterized and the skin of the abdomen is prepared in the usual manner. A median infraumbilical incision is made, the peritoneum is incised, and the abdominal cavity is walled off by laparotomy pads. A hypodermic injection of  $\frac{1}{2}$  c.c. of pituitrin is given. The uterus is mesially incised in its lower segment and the baby is delivered either by podalic version, cephalically (two fingers in the mouth) or by forceps. The placenta is then delivered manually, the uterus tamponed with iodoform gauze and the incision closed in three layers, two layers of continuous chromic catgut No. 2 for the muscle and a continuous Lembert suture of No. 1 chromic catgut for the visceral peritoneum. A cigarette drain is then placed directly over the wound on the uterus and made to exit at the lower angle of the abdominal incision. The drain is held in position by looping a few interrupted plain catgut No. 0 sutures around it, the sutures passing through the subjacent anterior uterine wall. This catgut is absorbed in from twenty-four to forty-eight hours and should it for some reason be necessary to remove the drain, there would probably be no sutures hindering removal after twenty-four hours. In my two cases, I removed the drain on the sixth day after operation, but, if desired, it could have been removed with safety on the third day.

#### CASE REPORTS

CASE 1.—Mrs. A. L., thirty years of age, born in Germany, admitted to Lebanon Hospital on April 1, 1925. She had several attacks of acute articular rheumatism while in Germany and was told that she had heart disease. The history on admission states that the patient is a primipara and has been in active labor at her home for about thirty hours. Her family physician who was in attendance at this labor had made several vaginal examinations without the use of gloves. Examination revealed a very stout, florid, female in active labor. The heart showed moderate hypertrophy, and a loud systolic murmur heard at the apex and transmitted to the left. There is also a presystolic murmur, heard at the apex accompanied by a palpable "thrill." Pulse 130. Full term pregnant uterus, vertex below and unengaged, fetal back to the left and heart heard in the left lower quadrant, 160.

Vaginal examination at the patient's home revealed the fetus in the L. O. A. position and the head unengaged, cervix four fingers' dilated, membranes ruptured, pelvis generally contracted.

On arrival at the hospital she was immediately taken to the operating room and under local anesthesia (novocaine 1 per cent) I performed a cesarean section employing the modified technic as described above. In addition I placed a small drain in the lower angle of the wound extending into the bottom of the vesicouterine space. This latter drain was removed on the third day postoperative.

Immediately after operation her hemoglobin was 75 per cent (Dare), systolic blood pressure 134. Her convalescence was satisfactory, and on the fourteenth day after operation she was discharged from the hospital. At this time the abdominal wound was healed except for a small granulating area at the lowermost angle. I have seen the patient since and her wound is entirely healed. There is no evidence of any hernia; the uterus is normal in size, position and consistency. The adnexa is normal.

CASE 2.—Mrs. M. Y., thirty years of age, admitted to Lebanon Hospital, Nov. 19, 1925. Family history is irrelevant. Patient had a laparotomy performed for uterine displacement. Does not know nature of the operation. Has one living child eight years of age and three years ago had a premature labor in the eighth month of gestation. The nature of the operative delivery employed in delivering her of this premature infant, she does not know but states that after this procedure she was "poisoned," remained in bed for six weeks, and had three blood transfusions. In the last three years she has had two miscarriages.

Patient began to have labor pains at 1 A.M. on morning of admission. She was admitted to the hospital at 10 P.M. At that time her family physician found the cervix thick and leathery and two fingers dilated. Membranes were intact. He ruptured her membranes the next day and cervical dilatation at this time was three fingers, but the cervix was still thick and leathery. The pains were weak and ineffectual. She received several doses of morphine sulphate hypodermically. She slept and appeared rested, but the cervix neither softened nor did the pains become effective. Because of the previous deliveries *per vaginam*, we decided to treat her conservatively. After three days of labor with the cervix still thick and leathery, however, the patient gradually becoming exhausted and the fetal head still unengaged, operative delivery was considered. The patient was very anxious to have a live baby and would not consent to any procedure that would risk the life of the child. Patient was operated upon under local anesthesia (1 per cent novocaine) supplemented by gas oxygen. The modified technic as outlined above was followed and in addition a small cigarette drain was inserted into the anterior culdesac. While closing the uterine incision, it was noted that the muscle in the lower one-third of the wound was exceedingly thin. The abdominal wound was closed, as is usual, in layers.

At the time of operation a culture taken from the interior of the uterine cavity contained hemolytic streptococci. Two days later a culture taken from the gauze portion of the cigarette drain overlying the uterine wound also contained hemolytic streptococci. Six day after the operation the abdominal wound at some distance from the drain broke down and cultures from this area contained hemolytic streptococci and *Staphylococcus aureus*. Drain to pelvis was removed three days after operation and uterine drain eight days after operation. On irrigating the uterine drain tract with acriflavine solution because of the presence of a purulent discharge, the irrigating fluid was noted to come out from the vagina. Vaginal examination by means of a speculum showed that this fluid was coming from the cervix, thus confirming the presence of a uterine fistula. The patient made an excellent recovery, leaving the hospital on the fourteenth day after operation, and her convalescence was fairly comfortable. Postpartum examination on Jan. 9, 1926, revealed a well-healed abdominal wound, uterus normally involuted, in normal position and freely movable. Adnexa normal.

#### SUMMARY

A preliminary report is presented of a modified technic for the performance of cesarean section in patients who are presumably infected.

Two cases are reported in which this technic was employed, in one of which cultures revealed the presence of hemolytic streptococci at the time of, and subsequent to, the operation.\*

\*NOTE: The writer has since operated by this technic on five additional presumably infected cases, with good results for both mother and child.

A uterine fistula occurred in the case showing hemolytic streptococci. Undoubtedly numbers of these organisms and infected material escaped through the hole in the uterus, but the tract formed by the uterine drain offered an avenue through which the noxious elements could escape.

Both patients recovered and postpartum examination revealed normal genital organs.

1272 GRAND CONCOURSE.

#### A CLINICAL STUDY OF ONE HUNDRED AND THIRTY-THREE PREGNANCIES FOLLOWING CESAREAN SECTION\*

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THE woman who has had one pregnancy terminated by cesarean section, and again becomes pregnant, presents a very real clinical problem. With the present rather widespread tendency to resort to delivery by abdominal section on account of numerous indications, other than contracted pelvis, more and more women present themselves each year requiring a decision as to the management of subsequent pregnancies.

The fundamental question involved, of course, concerns the behavior of the uterine scar in the pregnancies following cesarean section, and whether this scar will break down as a result of the strain to which it is subjected, with the attendant disastrous consequences to mother and child. This accident has occurred on numerous occasions and one line of treatment to prevent its occurrence has been suggested, namely, that every woman who has once been delivered by cesarean section should have all subsequent pregnancies terminated in a similar manner, or as it has been tersely expressed, "once a cesarean, always a cesarean."

In this connection a number of questions naturally arise. Is such radical treatment always necessary in the treatment of subsequent pregnancies occurring in these patients? and as a corollary to this, how real is the danger of rupture of the uterine scar? and again, is it possible with the present methods at our disposal to select the patients in whom rupture of the uterine scar is particularly likely to occur?

In the hope of being able to suggest reasonably satisfactory answers to these questions, I have analyzed the results obtained in all the cases of pregnancy following cesarean section occurring in the Johns Hopkins Hospital for a period of twenty-three years, from 1902

\*Presented before the Buffalo Academy of Medicine, March 17, 1926.

to 1925. While realizing that this has been a much discussed subject, the very frequency of its discussion and the variety of views presented indicate that satisfactory answers to the questions involved have not yet been obtained. Nearly all of the reports presented up to the present time have included only comparatively small series of cases, or have represented collections of cases from various sources. It was felt, therefore, that the presentation of a fairly large series from a single clinic might prove of value in properly evaluating the questions involved. During the period covered we have had the opportunity of observing 133 pregnancies following cesarean section; these pregnancies occurring in 100 women. In the majority of instances the original operation was performed in this clinic, but in a number of them it had been done elsewhere. Included in this material are the series of 10 cases recorded by Whitridge Williams in 1917, in his study on the healing of the uterine cicatrix, as well as the series of 64 women reported by Gamble in 1922. With this increased material we are now in a position to make a more extensive clinical study of the questions involved, and to decide whether conclusions previously drawn are correct or are in need of revision.

In our entire series, 73 women were observed in a single pregnancy following the original operation, while 21 were observed in two, and 6 women in three pregnancies subsequent to cesarean section. If we now proceed to a consideration of the mode of termination of these pregnancies and the end-results obtained, a number of points of interest are encountered. I shall consider first that group in which cesarean section was repeated in the subsequent pregnancies.

A high percentage of the women in our series presented varying degrees and types of pelvic deformity, the disproportion between the size of the pelvis and the presenting part of the child giving the indication for the original operation. Where marked disproportion was again present in subsequent pregnancies, delivery by cesarean section again became the procedure of choice. It should be noted, however, that this procedure was also elected in four women with normal pelvis on account of other indications; namely, once for premature separation of the placenta, once for nephritis, and twice on account of the age of the patients. In this series, the operation was repeated once in 52 instances, while in 15 women it was repeated twice, and in 2 others three times. In these 88 operations performed on 69 patients there were three maternal deaths, a mortality of 3.4 per cent. Inquiring into the causes of death in these patients, I find that in one instance it was due to hemorrhage, in another to general peritonitis following a conservative operation done late in the second stage (operation performed twenty years ago), while in the third it was due to general peritonitis following an intestinal injury which occurred

on account of dense adhesions between the intestines and the uterine scar of the previous operation. This latter death is one which must be directly attributed to the repeated cesarean section, and the increased difficulty which may attend the procedure on account of the possible presence of dense adhesions.

The formation of adhesions following cesarean section is in our experience a very frequent occurrence, and while, as Gamble pointed out, they occur more frequently in those patients who exhibit a febrile puerperium following the operation, yet they are also encountered with an unfortunate frequency in patients who have presented a most satisfactory convalescence. Often they are of a delicate filmy nature, and give rise to no discomfort to the patient, and cause no particular difficulty at subsequent operation. A frequent type of adhesion noted was that of the single rather broad band, extending from the site of the uterine incision to the anterior abdominal wall. This particular type of adhesion probably does no great harm, but rather may serve as a suspensory ligament to the uterus. In a number of our patients it was noted at the time of their discharge from the hospital that the uterus was definitely adherent to the lower angle of the abdominal scar and yet these patients when seen some months later were found to have quite movable uteri, doubtless due to the stretching of this adherent band, a situation comparable to that observed, following the old operation of ventrosuspension.

Again, adhesions between the uterus, omentum, peritoneum, and intestines may be quite generalized and very dense. Such a condition naturally adds greatly to the difficulties of a subsequent operation, and incidentally increases its risk. Even the low cervical operation may be followed by this complication. From the above findings it may be seen that repeated cesarean section is not to be regarded as an entirely innocuous procedure.

Let us now consider the results obtained in the case of patients who were delivered by the natural passages, at or near term, following one or more cesarean sections. This group comprises 29 women, in whom 39 deliveries occurred. In addition 9 spontaneous labors occurring in this group of women were cared for elsewhere, but in the absence of accurate records they have not been included for consideration in this series.

The original operations were performed on account of various indications. In a number the operation had been done on account of disproportion in women presenting moderate degrees of pelvic contraction. In the subsequent pregnancies the children were smaller, disproportion was not present, and labor was allowed to proceed. (Brief records of the case histories of several of these patients showing points of special interest are appended.) In other patients cesa-

rean section had been performed on account of such indications as antepartum hemorrhage and eclampsia, in women presenting normal pelvis. In the patients under consideration 25 pregnancies terminated spontaneously, 11 were delivered by low or mid forceps operations, and 3 by version. It is also of interest to note that 4 women in this group were each delivered three times subsequent to the cesarean section.

When the results obtained in this group are considered, we find that from the maternal standpoint they were uniformly excellent. There were no maternal deaths and no evidence of injury to the uterine scar. From these findings it is at once obvious that in this group of women repeated cesarean section was quite unnecessary from the maternal standpoint.

Considering the end-results from the standpoint of the child in this same group, we find that seven children were born dead or died within two weeks, a fetal mortality of 17.9 per cent. This would seem to be an unusually high figure, but on examining the individual records, we find that in only one instance did death occur in a full-term child, all the other deaths being in premature infants weighing less than 2400 gm. at birth. The single dead-born full-term child was delivered by low forceps after a five hour labor. Death was due to intrauterine asphyxia and may be fairly attributed to the effect of the delivery.

The proportion of premature infants in this group would appear to be unusually large, but considering the entire series they represent an incidence of 4.6 per cent. Furthermore, of these premature infants, two were born to women suffering from nephritis and one from syphilis, factors which definitely contribute to prematurity and death. It would scarcely seem justifiable, then, to draw the conclusion that cesarean section in one pregnancy predisposes to premature birth in subsequent ones.

That most serious of obstetric accidents, rupture of the uterus, occurred three times, an incidence of 2.2 per cent, which is a figure somewhat below those of Rongy and Eardley Holland, who placed the incidence of this accident at 3 per cent and 4 per cent respectively. The records of these three patients present a number of points which justify a more detailed presentation.

The first patient (Case 21 cited by Gamble) was a twenty-four-year old black multipara, with a generally contracted rachitic pelvis, diagonal conjugate 9.5 cm. Her first pregnancy ended in premature labor. At the end of her second pregnancy, a conservative cesarean section was performed in this clinic, this being followed for ten days by a febrile puerperium. In the seventh month of her third pregnancy she suddenly complained of rather severe abdominal pain. A day later, following slight vaginal bleeding, she walked to the hospital, a distance of more than half a mile. After admission, she was operated upon supposedly for a pelvic tumor complicating

pregnancy. On opening the abdomen, however, it was found that the uterus had ruptured through the previous cesarean scar, allowing the entire product of conception to escape into the abdominal cavity, where it formed a mass lying posterior to the uterus, which had been diagnosed as a pelvic tumor prior to operation. Little or no blood was found in the peritoneal cavity. Supravaginal hysterectomy was followed by an uneventful recovery. Striking features in connection with this patient were the very slight symptoms following the rupture, and the lack of bleeding and shock. Examination of the specimen revealed the fact that union following the first operation was defective, including only a bridge of decidua and peritoneum, this defective cicatrix rupturing as a result of the uterine distension. The placenta lay anteriorly.

The second patient (J. H. H., No. 12440), a twenty-two-year old white woman had a moderately contracted pelvis with a diagonal conjugate of 11 cm. Her first pregnancy had been terminated by a conservative cesarean section in another hospital. As far as could be learned the puerperium was afrebrile. At the end of her present pregnancy, little or no disproportion being present, she was allowed to go into labor. After seven hours of strong pains practically no dilatation of the cervix had occurred. This fact made it apparent that the uterine cicatrix would be subjected to an undue strain if labor were allowed to continue, so abdominal section was decided upon. On opening the abdomen it was found that the scar of the previous operation was just beginning to break open, this break extending a distance of about 3 cm. in the upper angle of the old scar. A living child was delivered and the patient made an uninterrupted recovery following supravaginal hysterectomy. The placenta lay posteriorly and in the fundus.

The third patient in whom this accident (J. H. H., No. 14171) occurred was a white woman, nineteen years of age, with a normal pelvis. Her first pregnancy was terminated by cesarean section in another hospital on account of eclampsia. The course of her convalescence could not be learned. She was admitted to the hospital at the end of her second pregnancy, not in labor, but complaining of rather vague abdominal discomfort, and showing no signs of shock. Shortly after this she complained of intense shoulder pain, and after another short interval signs of internal hemorrhage made their appearance. Immediate operation revealed an extensive rupture through and beyond the scar of the previous operation, which permitted the child and placenta to escape into the abdominal cavity. Supravaginal amputation of the uterus was done, but the patient died on the third day from bronchopneumonia. Examination of the specimen showed evidence of imperfect healing following the first operation.

The symptom of shoulder pain is one which is not always present in the case of rupture of the uterus, and is a symptom which I do not recall having been mentioned as being of significance in this condition. From the work done on insufflation of the peritoneal cavity, we now appreciate the meaning of this symptom. I would, therefore, suggest that when present, it is a symptom of definite diagnostic value in the condition of ruptured uterus, particularly in those patients in whom examination is difficult or unsatisfactory.

Completing this series are three women whose pregnancies terminated in abortions. Only one of these was spontaneous; the other two being performed for therapeutic reasons. It is unnecessary to comment further on this group, although one might be justified in

noting that the incidence of abortion is apparently not increased following cesarean section. The general results are summarized in Table I.

TABLE I

RESULTS OBTAINED IN 133 PREGNANCIES FOLLOWING CESAREAN SECTION IN 100 WOMEN

MODE OF TERMINATION	NO. OF INSTANCES	PER CENT	NO. OF WOMEN	MATER- NAL DEATHS	MATER- NAL MOR- TALITY	FETAL DEATHS	FETAL MOR- TALITY
A. Repeated Cesarean section	88	66.16	69	3	3.4%	5†	5.6%
B. Delivery by natural passages	39	29.32	29	0	0	7**	17.9%
C. Rupture of the uterine scar	3	2.25	3	1	33.3%	2	66.6%
D. Abortion, spontaneous and therapeutic	3	2.25	3	0	0	—	—
Total	133		104*				

\*Apparent discrepancy due to the fact that four women fall into more than one group.

†Three deaths due to premature separation of placenta, and Nephritis.

\*\*Six premature infants.

After studying this series of pregnancies following cesarean section, it becomes evident that rupture of the uterine scar is a very definite possibility, although a rather infrequent one. Is this a preventable accident, and what rules can be formulated to guide us in the management of subsequent pregnancies? In the case of women who present marked degrees of pelvic contraction, the treatment in subsequent pregnancies is obviously to repeat the operation, but what should be done in the case of the woman in whom the original operation was performed on account of some temporary indication? If we accept the dictum that all such women should have all subsequent pregnancies terminated by repeated cesarean section, two points I think have been made fairly obvious in this series: first, that we would perform an unnecessarily large number of cesarean sections, and second, that even then we would be unable to prevent a certain percentage of ruptures from occurring. In support of this latter statement, I would direct attention to the patient in our series in whom rupture occurred during the seventh month. Moreover, Findley found in his collected series of 53 cases of ruptured uterus following cesarean section that in 20 per cent of them the rupture occurred between the seventh and the eighth and a half months of pregnancy. Nor does the low cervical operation remove the menace, as is indicated by the reports of rupture following this operation which are appearing in the literature. Consequently it would seem that the only possible way to secure 100 per cent prophylaxis would be to terminate all such pregnancies prior to the seventh month, an obviously absurd suggestion. Furthermore, we

cannot ignore the fact that added difficulty, and added risk may attend repeated cesarean section, and we cannot agree with Newell that the risk of rupture is greater than that attending the repeated operation. Expressing the situation in figures, we might say that if 100 women delivered by cesarean section on account of some temporary indication were allowed to go into labor in a subsequent pregnancy, we might expect rupture of the uterine cicatrix to occur in three instances, with one maternal death, a mortality certainly no greater than that attending the repeated cesarean section. In suggesting any rules for our guidance in the treatment of these patients, it is realized that our present knowledge is not sufficient to guide us to an accurate decision in all cases, and that in each instance the decision will have to be made after all factors in the individual case have been considered. With this in mind, the following suggestions are offered as affording a maximum of safety and prophylaxis to such patients.

1. *Patients presenting definite mechanical obstruction; such as a marked degree of pelvic contraction, who have had one pregnancy terminated by cesarean section, should have all subsequent pregnancies terminated by the same procedure.* In order to reduce to a minimum any possible danger of rupture, the accident so often occurring at the end of pregnancy or at the beginning of labor, the repeated operation should be an elective one, preferably a week or ten days before the expected date of confinement. This should apply particularly to such women as have shown evidence of infection after the original operation. Such patients should be kept under the closest possible supervision throughout their pregnancy, the rate of growth of the child and the development of uterine distension being carefully watched. It is particularly desirable that such patients should be in a hospital for two weeks prior to the expected date of confinement.

2. *In the case of patients who have had one pregnancy terminated by cesarean section on account of some temporary indication,—and such patients form an increasingly large group,—the decision as to the procedure to be followed in subsequent pregnancies is more difficult.* It would seem, however, that our safest guide at present would be to base the decision upon the character of the puerperium following the original operation. If definite evidence of infection be present, poor healing of the uterine wound is likely, with the production of a cicatrix which is poorly adapted to withstand the strain of labor, or even the distention incident to the last weeks of pregnancy. In this group, repeated cesarean section would be the procedure of choice in a subsequent pregnancy, and again this should be carried out as an elective procedure according to the suggestions laid down for the first group. A question that suggests itself in the conduct of the repeated operation in this group is the possibility of completely excising the defective scar, in the hope of obtaining a firm resistant cicatrix.

In those patients in whom the puerperium following the primary operation presented an afebrile course, one may reasonably presume, as shown by Whitridge Williams, that a satisfactory union of the uterine wound has taken place. In this group labor may be allowed to proceed, although realizing that even then an occasional rupture through the scar may take place. It seems probable that the occasional rupture occurring in this group of patients is more likely to be due to defective union following faulty suturing than to an infection giving rise to no signs or symptoms. Such factors as the age of the patient, and particularly the state of rigidity of the cervix, should also be most carefully considered in attempting to determine how much strain is likely to be thrown on the uterine cicatrix.

An incidental question that arises in the case of women with a marked degree of pelvic contraction who necessarily must have all full-term pregnancies terminated by cesarean section, is in regard to the number of times the operation should be repeated. In this connection, I might say that it has always been our custom to sterilize, at any cesarean section, those patients presenting a vital indication, whose lives would be distinctly menaced by subsequent pregnancies. In the absence of such vital indication, it has been our habit to sterilize the patient at the second operation if she so requests, provided the first child is alive and well. In the case of the patient presenting herself for the third operation, we usually advise sterilization, feeling that such a woman has fully performed her duty to society and is not justified in subjecting herself to further risks. This advice is not always accepted, and each of two women in our series have been delivered four times by cesarean section.

In conclusion, it seems fair to state that the dictum "once a cesarean, always a cesarean" does not necessarily hold true. The line of treatment to be followed in any case of pregnancy following cesarean section will have to be decided on its individual merits. The great majority of women in whom the primary operation was performed on account of some temporary indication, may be safely allowed to go into labor in subsequent pregnancies, and if those cases be excluded, which have presented a febrile puerperium after the original operation, or who present undue rigidity of the cervix, the risk will be minimal.

#### CASE HISTORIES

##### A. *Several deliveries by the natural passages after one cesarean section.*

CASE 1.—J. H. H., No. 14496, twenty-seven years old, black, generally contracted typical pelvis, diagonal conjugate 11.25 cm. First pregnancy terminated by cesarean section at another hospital; child stillborn. Second pregnancy terminated spontaneously after a twenty-three and a half hours labor; the third ended spontaneously after six and a half hours, while the fourth, attended by a midwife, also ended spon-

taneously after a short labor. In the fifth she was again treated in this clinic and again had a spontaneous labor after three and three-quarter hours.

All the children were born alive, and the three born in this clinic weighed 3,000 gm. or over. The points of particular interest lie in the number of pregnancies following the original operation, and the duration of the first labor.

**CASE 2.**—J. H. H., No. 13876, twenty-five years old, black, generally contracted rachitic pelvis, diagonal conjugate 10.5 cm. First pregnancy terminated by cesarean section on account of eclampsia; child stillborn. Second pregnancy terminated by low forceps after a nine and three-quarter hour labor; child weighed 3230 gm.; condition excellent. Third pregnancy terminated by podalic version at beginning of the second stage; child weighed 2620 gm; condition excellent. Fourth pregnancy ended spontaneously, a premature labor, lasting eleven and a half hours. Child small, weighing 1545 gm., but did extremely well.

**CASE 3.**—J. H. H. No. 11533, thirty-four years old, black, generally contracted rachitic pelvis, diagonal conjugate 10.25 cm. One ectopic pregnancy, and four early miscarriages prior to her first full-term pregnancy. First full-term pregnancy was terminated by conservative cesarean section at the onset of labor, on account of her pelvis and an associated prolapsed cord. Child weighed 3500 gm., condition excellent. The next pregnancy ended spontaneously after twenty hours, child weighing 3800 gm., condition excellent. There was no disproportion, although the child was of large size. The next two pregnancies also ended spontaneously after twelve hour labors, and resulted in living children weighing 3,000 gm. each. Four spontaneous labors after one cesarean section.

**CASE 4.**—J. H. H., No. 14089, twenty-five years, black, normal pelvis. First pregnancy terminated by conservative cesarean section in another city for unknown indication; a living child. Second pregnancy ended by a forceps operation by private physician; child died on third day. Third pregnancy ended in spontaneous labor in this clinic after four and a half hours. Child in excellent condition, unusually large, weighing 4630 gm. Fourth pregnancy terminated by induction of labor, on account of large child and a pregnancy apparently beyond term. After induction of labor by a bougie, spontaneous labor occurred after four and three-quarter hours, the child weighing 4065 gm. The large size of the children is of interest in this patient.

#### *B. Delivery by natural passages after two cesarean sections.*

**CASE 5.**—J. H. H., No. 14084, twenty-two years old, black. Pelvis kyphotic, oblique funnel, diagonal conjugate 11.75 cm., transverse 7.75 cm., kyphosis in upper dorsal, and also in lumbar regions. The first two pregnancies were terminated by conservative cesarean section in another city. First child alive, second died on first day. Subsequent pregnancies treated in this clinic. The third was terminated by a low forceps operation after a four-hour labor. The child weighed 2420 gm., condition excellent. The fourth pregnancy was also ended by a low forceps after four and three-quarter hours of labor. The child, weighing 2800 gm. was asphyxiated and could not be revived. The fifth was terminated in a similar manner after a nine and a half hour labor. The child weighed 3010 gm., condition excellent.

**CASE 6.**—J. H. H., No. 13818, twenty years old, black, generally contracted rachitic pelvis, diagonal conjugate 10.5 cm. First pregnancy terminated by conservative cesarean section on account of disproportion. Child weighed 3260 gm., condition excellent. Second pregnancy also terminated by a similar procedure; child weighed 3490 gm., condition excellent. Both operations were performed in this

clinic. In the third pregnancy no disproportion being apparent, she was allowed to go into labor. This ended spontaneously after nine hours. The child weighed 3225 gm., condition excellent.

The following case is cited as a particularly good example of a contracted pelvis in which a difference in the size of the child was responsible for the different line of treatment followed in the second pregnancy.

CASE 7.—J. H. H., No. 13352, twenty-two years, black, generally contracted rachitic pelvis, diagonal conjugate 10.25 cm. First pregnancy terminated by conservative cesarean section at the onset of labor on account of disproportion. The child weighed 2740 gm., condition excellent. In her second pregnancy, there was no disproportion present, and spontaneous birth of a living child, weighing 2360 gm. occurred after thirteen and a half hours of labor. Treatment in subsequent pregnancies would depend largely on the size of the baby. A large child would obviously have to be delivered by a repeated cesarean section; whereas in the case of a small child, spontaneous labor might again occur.

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# Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D.

## THE COMMITTEE ON MATERNAL HEALTH

*Organization and Plans.*—The Committee on Maternal Health, controlled by and under the direction of physicians, was organized March 9, 1923, to undertake a scientific investigation of contraception, sterilization and general problems of sterility and fertility from a medical and public health point of view. While it recognizes the importance of the ethical or moral and the economic considerations involved, the Committee aims to confine itself to the medical aspects of these questions.

The Committee's working plan has been approved by the American Gynecological Society, the New York Obstetrical Society, and the Public Relations Committee of the New York Academy of Medicine.

*Organization.*—The members of the Executive Committee who are directly responsible for the organization's activities are as follows: Doctors Samuel W. Lambert, chairman, Robert L. Dickinson, secretary, Haven Emerson, Robert T. Frank, Frederick C. Holden, George W. Kosmak, James Pedersen, and William F. Snow, Mr. Bailey B. Burritt, Mrs. Gertrude Pinchot, and Miss Marguerite A. Wales.

There are two active subcommittees: one on medical service, which is in charge of the clinical investigation outlined below—Dr. Frederick C. Holden, chairman, Dr. William E. Caldwell, and the secretary; and one in charge of research—Dr. Robert T. Frank, chairman, Dr. Herbert M. Evans of the University of California, Dr. C. R. Stockard of Cornell University, and the secretary. Dr. G. W. Kosmak serves as a committee of one to advise on publications.

As it has seemed increasingly important to attempt to determine or at least to study and discuss the medical indications for contraception and sterilization to the end that the medical profession may more fully recognize contraception as a preventive measure, the Committee is at present organizing a subcommittee on medical indications. Dr. Nellis B. Foster will be chairman of this committee, which proposes as an initial undertaking to draft and submit for medical comment and criticism a tentative list of medical indications for contraception.

There is a medical advisory group who are from time to time consulted on policies and procedures. There are also advisory, legal, nursing, and lay groups. The recently employed full-time executive secretary is a physician.

The work of the Committee has been supported by voluntary contributions. One of the Foundations has assisted with funds for research.

The office of the Committee is at 370 Seventh Avenue, New York City, in the same building with various national health organizations.

*Clinical Investigation.*—Part of the work that the Committee has undertaken is a clinical study of contraception in which the following New York Hospitals are cooperating: Lebanon, Lenox Hill, Jewish, Mt. Sinai, New York Infirmary for Women and Children, New York Nursery and Childs, Sloane, and Woman's Hospitals.

The purposes of the clinic service are: (1) to provide medical service for women needing contraceptive advice "to cure or prevent disease" as permitted under the

New York State Law; (2) to gather evidence as to indications, i.e., conditions under which advice for or against pregnancy shall be given, including application of sterilization; (3) to gather a series of histories of patients who are using various contraceptive methods under medical advice and supervision; the analysis of such histories to provide evidence as to the efficacy, harm, or harmlessness of the several methods.

The collection of such a series of case histories under the supervision of physicians in institutions of high standing is essential if the medical profession is to be able to speak with any degree of scientific accuracy about questions such as the following:

What are the physiologic and psychologic effects of contraception upon the individual?

What are the effects of contraception upon subsequent fertility?

What is the relative value of contraceptives as to reliability, simplicity, and harmlessness?

The Committee on Maternal Health through hundreds of interviews both in Europe and America has secured a great deal of valuable opinion upon those questions, but the opinions differ widely. They are therefore making an unbiased clinical investigation of the facts. They are keeping a uniform history. They have offered an honorarium to clinic physicians in order to secure complete histories. They aim to keep patients under supervision for at least a year. The method of choice where there are no contraindications is the Mensinga Pessary plus contraceptive paste. The progress in securing such case histories is slow so as to conform to the New York State Law. The clinics strictly limit their service to patients who present medical indications for contraception.

*Research.*—The Committee's three main objectives in the domain of research have direct bearing upon the problems both of sterility and fertility, namely: (1) spermatoxins; (2) when does human ovulation occur, and (3) the period of receptivity in the female.

The subcommittee on research is studying this field and has been able to promote, and in some instances to assist financially, with the study of these problems. When it is able to secure further financial assistance it proposes to increase its research activities. Needless to say in this field even more than in its clinical investigation the Committee expects no immediate or startling results.

*Other Activities.*—Some of the other activities of the Committee on Maternal Health are:

1. The abstracting and indexing of literature
2. The inspection of birth control clinics and their records
3. A critical survey of foreign experience and American practice
4. Furnishing clinics with supplies not otherwise procurable.

*Legal.*—As both our federal and state laws in differing degrees hamper physicians in giving contraceptive advice to their patients, the Committee has made some effort to secure consideration by organized medicine to the end that these laws may be amended.

The following suggested amendment has been submitted to and endorsed by the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association: "Resolved, that we hereby recommend the alteration of existing laws wherever necessary so that physicians may legally give contraceptive information to their patients in the regular course of practice."

Because the Postal Law forbids transmission of practical information and even medical publications concerning birth control, the following suggested amendment was submitted to and endorsed by the American Gynecological Society: "Standard

medical and scientific journals and reprints therefrom and standard medical works which contain information with reference to the preventing of conception are not nonmailable under this section."

*Conclusion.*—The Committee on Maternal Health realizes that in studying contraception they are entering a difficult field where they will meet with opposition not only from those who are biased or prejudiced but also from those who are sincerely opposed because of religious or ethical considerations. Their efforts to study sterility and fertility do not, of course, meet with these same difficulties.

The Committee, feels, however, that as every physician meets situations where he must consider contraception as a health measure, it is essential that the question be squarely faced as an important medical problem and receive proper scientific consideration.

### THE PHYSICIAN'S PART IN A PRACTICAL STATE PROGRAM OF PRENATAL CARE\*

BY FRED L. ADAIR, M.D., MINNEAPOLIS, MINN.

*(Chairman, Joint Committee on Maternal Welfare)*

**A** GOOD understanding of the significance and purpose of prenatal or antepartum care must be had before an attempt is made to elaborate an intelligent and practical program and to define the relationship of the physician to such a plan for the state. The word "state" in this article refers to the geographic or governmental unit and not to the abstract definition.

According to a committee which recently drew up some standards of prenatal care for the Children's Bureau, "Prenatal care is that part of maternal care which has as its object the complete supervision of the pregnant woman in order to preserve the happiness, health, and life of the mother and child. Therefore all pregnant women should be under medical supervision during their entire pregnancy, for it is only by careful routine prenatal care that pregnancy and labor can be made safer."

If we are created to create, and the chief end of man is man, dare one in this modern era say that maternity is the chief function of woman? The carrying out of this physiologic law is vital to the perpetuation of the human race, which we assume to be the desire of human beings.

We fully realize that much can be done by caring for mother and future offspring during the period of pregnancy. We are convinced, for instance, that congenital syphilis can be more effectually treated during pregnancy than during infancy, but no one doubts that it could be still more adequately handled prior to the onset of pregnancy itself. This specific instance illustrates the general principle that while much can be done by our present plan of prenatal care to preserve the happiness, health, and lives of offspring, this plan is too limited to fully accomplish the purposes which are promulgated. While we are striving to perfect and carry out universally the care of the pregnant woman we must also begin to enlarge our conception of prenatal care, or coin another name, such as anteconceptional care or preembryonic care.

Prenatal usually implies during pregnancy, but one is led to consider when prenatal care begins, and though we may not accept the name we must recognize the fact that causes operate to affect the offspring for good or ill prior to the fertilization which leads to the ultimate development of an individual.

\*Read at the Third Annual Conference of State Directors of Maternity and Infancy Work, Washington, D. C., January 11, 1926. For complete paper, see official report.

Can we check the increase of defectives by care of the pregnant woman? Which type of prenatal care is more sane and far-reaching in its results; that which is applied to defective individuals during the anteconceptional or preembryonic period and prevents the natural increase of such individuals, or that plan which humanely surrounds these poor defectives who are prospective mothers by good prenatal care but hopelessly inadequate so far as final results are concerned?

Consider also the fact of skeletal development and the elimination of rachitis in its relation to childbearing. Can one estimate the tremendous importance of the universal elimination of this disease on childbearing and its value in preserving the happiness, health, and lives of both mother and offspring? In the same manner, the prevention of faulty nutrition, of improper hygiene (both physical and mental), and of disease would forestall many unhappy results which ensue in later life and lead to handicapped mothers and offspring.

It might seem almost useless to talk of the hackneyed subject of venereal disease,—its cure and prevention, if it were not almost an everyday occurrence to see the dire results of gonorrhreal and syphilitic infection on both mothers and offspring. It is useless to think of accomplishing the purposes of prenatal care by treatment of these diseases during pregnancy. Such therapy at times cannot be avoided. The laity should understand and the medical profession realize more fully the necessity for curing these diseases prior to the onset of pregnancy and make such procedures a more general practice.

Much good could be accomplished for both parents and offspring if careful histories and physical examinations of potential fathers and mothers could be effectively made before conception took place. This would be in line with the idea of periodic physical examinations, but the viewpoint would be somewhat different. The idea back of the periodic health examination is, of course, the welfare of the individual; but here we would take into consideration not only the health of the prospective parent but also that of the future offspring. This brings us to the point of the future father and his relation to the happiness, health, and even life of both his wife and offspring. This parent has been largely ignored in prenatal plans and yet he is responsible for a great deal of damage, some of which could be avoided by the proper inclusion of this individual in the prenatal program.

We now come to a consideration of the care of the prospective mother. Proper prenatal care includes much more than the physician can supply to the future mother. Everything to make a suitable environment, assuring good hygiene, proper nutriment, appropriate work and recreation, should be provided. No physician, even granting that he has the requisite knowledge to advise properly, could furnish all the social and economic desiderata to his patients.

A very important part of any prenatal plan is the guidance of mothers in making the most of everything they have, and in case of need in assisting them to secure the necessities which they lack for themselves and the future baby. This is, of course, somewhat aside from the physician's part in the plan, but it is vital for the success of his work and for the welfare of his patients. It is highly desirable that the physician make it a point to see that some contacts are made by the patient so that these needs are met. This is, in fact, almost vital for the proper working of the prenatal plan as well as for the natal and postnatal care. The physician's main task is that of looking after the health of his clientele, but the idea of healing the sick has been so thoroughly ingrained that it is difficult to inculcate the idea of prevention into lay and medical minds. Unless one grasps the idea of prevention as applied to obstetrics there will be no comprehension of prenatal care. Unfortunately not all catastrophes can be prevented even though foreseen.

The first part the physician plays in a practical prenatal plan is his individual relationship to the prospective mother. His first effort should be to secure the con-

fidence of his patient and assure her of his interest in her welfare by a careful consideration of her problems and a study of her case.

When a patient is first seen a good history should be taken so as to bring out the past events in her life. Facts relative to her early development and nutrition should be elicited. History of previous diseases, such as scarlatina, diphtheria, rheumatic fever, tonsillitis, variola, tuberculosis, and venereal infections, should be obtained. Information as to previous vaccination is important as serious results for both mother and fetus may be prevented. Information as to the occurrence of conditions which have required surgical intervention should be secured. It is also important to obtain history of goiter, thoracic disease, and acute or chronic abdominal affections. The possibility of persistent foci of infection should not be overlooked. The sexual life of the woman should be observed from the standpoint of her puberal development and menstrual history. The character of previous pregnancies, labors, and puerperia is important, and this information may best be obtained by questions which will bring out the facts in chronologic order.

A careful physical examination should be made in order to establish the patient's status not only with reference to the pregnancy itself, but also to determine as accurately as possible the physical and mental condition of the woman. The patient must be seen repeatedly during pregnancy in order to oversee and supervise her intelligently. Final obstetric examination should be made a few weeks before the date set for confinement in order to determine the condition of the mother and the size and position of the fetus.

It is not necessary to go into details regarding the hygiene of pregnancy as the main facts are, or should be, common knowledge. Any physician should know these facts, and if he does not it is easy for him to obtain them if he is interested. It is one of his functions in some way to provide the patient with this information. He must be continually on the lookout for abnormal conditions which are both accidental and incidental to pregnancy. It is part of the physician's task to secure the cooperation of his patient so that he may be informed at the earliest possible time of any symptoms indicating complications. It is only in this manner that events which lead to disaster to mother and offspring can be avoided during pregnancy. Last, but by no means least, the prospective mother must be shown the necessity and manner of preparing herself and her home, if necessary, for the reception of the newcomer. It is only during pregnancy that proper preparations can be made for the all important natal and postnatal care.

The physician also has a relationship to his community. He is granted the privilege of medical practice by the state and as a result he incurs certain obligations. The chief one of these is teaching and helping the community to prevent disease and death among its members. It should be one of his functions to co-operate in every way with the various agencies of his community in an effort to apply prevention to the practice of obstetrics. It is his duty to educate, and demonstrate by his methods of obstetric care that he knows the importance of the proper examination and observation of pregnant women.

There is also the specialist in obstetrics and the general practitioner or inexperienced obstetrician to consider. The experienced specialist should really not care for the routine and normal obstetric cases, but reserve his energy and ability for the more trying and hazardous cases. On the other hand, the practitioner and inexperienced obstetrician should not hesitate to secure the benefit of greater experience for the welfare of their patients.

The relation of the practitioner to clinics is of great importance. Many patients cannot afford to pay an adequate fee for prenatal, natal, and postnatal care. Some cannot pay for any of this service and should receive this care in a free or part pay clinic. Other patients are able to pay for part of the service and can employ a physician for this portion of their care. There should be the fullest cooperation

between the physicians and these clinics to the ultimate benefit of all concerned. There should be helpful teamwork between those who practice obstetrics and the maternity wards of hospitals so that complicated cases can be promptly hospitalized and cared for properly before it is too late to prevent disastrous consequences. Hospital facilities for the care of maternity patients have been and are woefully inadequate. Physicians should cooperate in plans to develop and improve such hospital facilities not only in large centers of population, but, even more important, in counties and small cities.

What the individual physician should do as outlined above, the medical profession should also do on a larger scale. The community should be educated to the necessity of prevention in general and to the importance of prevention of maternal and fetal mortality and morbidity. There is nothing more important to the community than the production and protection of normal human beings. Proper obstetric care as represented by prenatal care is one of the most important ways of accomplishing this result. The medical profession should be vitally interested in fostering a state-wide plan for carrying on this work. No plan of prenatal care can be successful in any state where the participation and cooperation of the medical profession is not secured.

Teachers and teaching institutions are indispensable in the carrying out of any state plan. Those already in practice need to be taught and kept abreast of obstetric progress. Specialists must be taught and trained through years of instruction. Practitioners must be prepared during the undergraduate course and the intern year. This means good teachers who are well trained and with adequate time and energy to make teaching their main work. It means also adequate teaching hours for obstetrics, adequate equipment, and patients who can be used clinically for demonstration without harm or discomfort to themselves or offspring.

There must, therefore, be close cooperation between officials and practitioners and the medical profession. The laity and physicians must understand each other. The former must realize that careful preparation and years of study are necessary qualifications, and the latter must know that the people wish real service which gives results. Obstetric practitioners must cooperate with each other and men must realize their limitations and recognize the qualifications of others along special lines. All should strive for better institutional facilities and organizations for maternity care. There should be closer contact between practitioners and teachers and teaching institutions. Investigators should be encouraged and supplied with material for study from all available sources. We should all realize the value of statistics and especially vital statistics, and cooperate to the fullest extent in securing accurate and valuable reports. It is also important that we recognize the desirability of certain changes in reporting termination of pregnancy, especially those which result in stillbirths and nonviable fetuses. Physicians should recognize the fields of activity occupied in prenatal work by nurses and social workers. Each should take pride in his own work and respect the ability and usefulness of those in other fields of activity so that all may work together in harmony for the preservation of the happiness, health, and lives of mothers and their offspring.

## Society Transactions

### NEW YORK OBSTETRICAL SOCIETY

MEETING OF MARCH 9, 1926

THE PRESIDENT, DR. O. PAUL HUMPSTONE, IN THE CHAIR

DR. ELIOTT BISHOP described an instance of **Malignancy in a Cervical Polyp.**

This patient was a sixty-eight-year-old widow with the classical complaints and signs of a complete prolapse. For a month she had had a little spotting; her general condition seemed as good as one would expect at her age. The uterus, a good deal of the bladder, and some of the rectum was out of the vulva; the cervix showed a small erosion, due, we presumed, to external contact and causing the slight spotting; we also noted a small polyp that seemed innocent. Palliative treatment in the dispensary had been of slight help, and her social condition seemed to demand a return to increased efficiency; therefore she was subjected to an amputation of the cervix and an interposition of the fundus. Her recovery was uneventful.

The pathologic report read "cervical polyp with basal cell carcinoma. Chronic endocervicitis." Microscopic section of polyp showed a malignant epithelial growth which took up practically the entire section. The epithelial cells were very irregular with numerous mitotic figures. No pearl formation was seen.

Immediate consultation was held, and it was decided to apply radium in six weeks, which was done, in spite of the narrowed vagina, using 100 mg. in an inverted T in the cervix.

Dr. Dickinson reports that of 106 recorded cases of polyp seen in private practice, most of which had histologic examinations, but one had malignancy. Upon this patient he did a Byrne cautery amputation of the cervix, and both Dr. Archibald Murray and Dr. James Ewing pronounced one polyp malignant.

From this one case, we may presume that the malignancy is not of high degree. The patient is living and well after twelve years, though she has had a very stormy time from dysmenorrhea caused by stenosis of the canal; she was treated before the days of radium, which would have produced a menopause.

Our case interested me to study the rarity of the condition. No case has been reported in the last eight years in the *Journal of the American Medical Association* and none in the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY* since it was founded. In *Surgery, Gynecology, and Obstetrics*, for the last eight years we find only one reference. In the number for August, 1921, Dr. N. Sproat Heaney of Chicago reported a case and said that he had one other nine or ten years before. Dr. Vineberg of Mt. Sinai Hospital told the writer that he had seen two or three in his practice. Frank in his *Gynecological and Obstetrical Pathology*, says that "malignant changes in polypi are not very frequent, but do, however, occur. \* \* \* The association (of cancer) with uterine polypi has never been subjected to numerical study. It has been repeatedly noted in beginning carcinoma (now quoting from Mortier, writing in *Progress Medical* in 1906) that the tip of the polyp shows carcinoma, the base being still benign." Previously he states that he "has repeatedly

seen polypi erroneously diagnosed as cancer. The examination of the base of the pedicle is decisive."

While gynecologists, in general, view this condition as a rarity, gastrointestinal observers in their field take a very different stand. Erdman and Morris in *Surgery, Gynecology and Obstetrics* for April, 1925, in a survey of polyposis of the colon, said that malignancy occurred in 40 per cent of the cases. Struthers from the Mayo Clinic in the same journal for May, 1924, and, previously, in *The Annals of Surgery*, in 1920, came to the conclusion that the disease terminated in malignancy in a large percentage of cases. Doerring has been quoted by Müller that, "of fifty known cases of intestinal polyposis thirty-one terminated in cancerous degeneration." While this is extrapelvic pathology, may it not be considered a suspicious signboard? In spite of Dr. Dickinson's figures, and Dr. Graves' flat statement, may we not ask, Is this such a rarity after all? Again let us ask, If we do not find this condition has it been originally malignant, or has it become malignant? Pathologists in general believe that cancer rarely takes a polypoid form; if so, we must believe that malignancy from irritation or other cause with some degree of frequency develops on a benign polyp. Its low degree of malignancy would also incline one to the latter view.

I think, however, that the obvious conclusion is that we should view every polyp with suspicion and subject it to histologic examination, the logical treatment to follow.

#### DISCUSSION

DR. HERMANN GRAD.—I had a patient with a fibroid and also a polyp in the cervix. I did a supravaginal hysterectomy and then I did not remove the cervix. I did not suspect that this polyp was malignant. Then I removed the polyp and the pathologist reported that it was malignant.

DR. H. D. FURNISS.—I believe it would be a very simple matter to treat most of these polyps as an office procedure, because fulguration will destroy them, and it can be done without any bleeding.

Recently I also had a case of sarcomatous changes in a rather large uterine polyp.

DR. W. P. CONAWAY.—In August, 1924, I removed a cervical polyp about the size of an English walnut from a nulliparous patient thirty-eight years of age. I curetted the uterus, snipped off the polyp with a pair of scissors, and used the actual cautery on the base. The pathologist reported malignant disease. At that time we had only 25 mg. of radium available, so I used that. I explained the condition to the patient, who was a nurse, and she preferred to take her chances. Since then there has been no irregular bleeding and she has been perfectly well. That is the only case we have had in over twenty years of service.

DR. W. H. CARY.—I saw Dr. Dickinson's patient, to whom Dr. Bishop referred, only yesterday, and she is perfectly well. A very interesting feature of her course following the cautery amputation of the cervix was that she developed an atresia of the cervix, hematometra and bleeding that certainly looked very much as if she might have an extension of malignancy in the fundus. She refused diagnostic curettage and also the use of radium, which was suggested some time subsequent to the time of Dr. Dickinson's operation. By dilatation of the cervix she finally drained gradually, her periods became regular and she reached the menopause about three years ago.

DR. JOHN O. POLAK.—Some years ago it was called to my attention that there were two types of polypoid growths which might become malignant. It is surprising to find a large incidence of sarcomatous malignancy in the fibroid polyp protruding from the cervix with its origin in the body of the uterus. The mucous polyp is

an innocent affair apparently, and here, again, by routine examination, you can find more than you would ordinarily suspect. We have found four of these cases of simple mucous polyps by routine pathologic examination in the last five years.

Furthermore, I am rather of the impression, from the report that our pathologist gives us, that these growths are increased or are changes that take place in the polyp rather than originating as a malignant growth in its incipency or in its beginning.

DR. S. H. GEIST.—At Mt. Sinai Laboratory we routinely examine all specimens removed. We have had occasion histologically to study cervical polyps removed both on the Gynecological Service and the Out-Patient Department and find that very rarely indeed do these tumors present malignant changes. It must be remembered that these pedunculated growths are subjected to a great deal of trauma and that practically all of them are infected. As a result one often finds metaplastic changes in the epithelium suggestive of malignancy, and consequently an error in diagnosis may readily be made. If one recalls the report of Dr. Ewing, read by Dr. Bishop, it will be noted that in it he stated that certain characteristics were lacking to make absolutely certain the diagnosis of malignant tumor.

It is true that these metaplastic changes with their atypical cells often mislead one in a diagnosis. From our experience we must conclude that malignant change in a cervical polyp is infrequent. About two or three years ago I published the report of a number of cases of cervical polyp that were very carefully studied histologically, and in no case was there found a true carcinoma.

DR. I. C. RUBIN.—One fact that explains the relatively infrequent malignant degeneration of the cervical polypi is the common practice of removing them early, because they frequently cause spotting and bleeding and are often encountered in young women. They are snipped off in the office and that ends them. Another reason is, perhaps, the fact that these polypi may be extruded even without the knowledge of the patient or without being removed by operation.

Dr. Geist's remarks are apropos, because early epidermization of cervical polypi is a common occurrence, and on routine cutting of these cervical polypi you see very frequently large islands of metaplastic epithelium or even epidermization.

There is no doubt but that the case reported by Dr. Bishop is a genuine case of malignancy, but one must pay attention to the histologic differences.

About ten years ago I reported a case of fundal polyp, on the apex of which an adenocarcinoma had formed, which was removed by the curette. There was a great deal of discussion in that case as to whether there was not a possible mixing up of the specimens in the laboratory. There was no doubt that the carcinoma had engrafted itself upon the apex of this submucous polyp and extended down from the fundus. Malignant degeneration of a cervical polyp is, however, an exceedingly rare occurrence.

DR. JAMES N. WEST.—I have removed a great many of these polypi since 1894, and I have always regarded them as innocent growths. I do not recall ever having seen a patient who developed carcinoma after removal of one of these polypi. So if this is truly a malignant process it must be of a peculiarly benign character which is not inclined to cause metastasis or involvement of the higher structures.

DR. W. E. DANNREUTHER read by invitation a paper entitled **The Preoperative Responsibility of the Gynecologist.** (See page 260.)

#### DISCUSSION

DR. FREDERICK C. HOLDEN.—I am inclined to think that the increased operative incidence, or increase of large operative incidence, is produced by several factors, as follows:

*Ignorance.* I believe that many men proceed, not knowing many of these very important things to which the doctor has called attention. They are unable to realize the relationship existing between the pathology and the symptoms, as he pointed out, and people receive unnecessary operations, although honestly so, at the hands of men who are not able to judge the cause of the symptoms. The result is that people are operated upon and a cure is not effected. I think there are still many of us who fall into that category.

Another cause of high operative incidence is *carelessness*. We know of these things, but we do not do them. We have large services, and, as a result, we become routine and neglect many of these things that make so much for success. In so far as our service at Bellevue, which is a large one, is concerned, our operative incidence covering a period of six years is under 22 per cent, and we attribute that principally to preoperative study. We are very fortunate there in not having to hurry operations. Patients never enter in afternoon to be operated upon in the morning. We have a longer time for preoperative study, which is absolutely necessary.

DR. JAMES N. WEST.—No matter how anxious we may be to carry out thorough examination, biochemical and otherwise, patients today expect to be operated upon quickly, and they demand it. It is also very difficult to get the average patient, especially what you might call a semiprivate or ward patient in the hospital, to come in several days before and have this proper preparation. Then, again, of course, the vast majority of our cases do not demand such careful investigations. Examination much less thorough than that suggested by the doctor is sufficient to demonstrate that the patient's heart and kidneys are sound and that they are surgically competent.

I thoroughly agree with him, however, on any case which shows an incompetent surgical history. For instance, if we have a case where the function of the kidney seems to be disturbed, where the patient seems to be toxic, where she has Bright's disease, diabetes, tuberculosis, high blood pressure, or vascular disease, then I believe she should be put through a thorough examination. I had a patient the other day, a woman who weighed 230 pounds, who was extremely anemic, and who had been bleeding profusely. I found 40 per cent hemoglobin. I did a supravaginal hysterectomy for a large fibroid tumor, which was mostly submucous, and never have I had a patient make a more satisfactory recovery.

I have been surprised to find that high blood pressure is not as much of a contraindication to operation as I had believed it to be. In the last two or three years I have been forced to operate upon several patients with high blood pressure, realizing or at least feeling that they were taking a pretty big chance. They recovered satisfactorily.

DR. HARBECK HALSTED.—The late Dr. Studdiford was always tremendously interested in this subject of preoperative study. We have a rule at Sloane that no patient shall be operated upon less than forty-eight hours after admission unless an immediate operation is absolutely essential. The wait in the hospital before operation is usually nearer a week.

The two principles which we have always followed are: patients should be in the hospital at rest for at least forty-eight hours before operation, and that we should use our medical consultant in all questionable cases.

Although I am tremendously interested in cystoscopy and was very glad to hear the doctor mention its importance, I believe it is not necessary to cystoscope every gynecologic patient.

DR. DANNREUTHER (closing).—I fear that I have been misunderstood. I do not advocate that all of the diagnostic tests to which I have referred should be done

as a matter of routine. On the contrary, on my service at the Post-Graduate Hospital even a Wassermann reaction is not done routinely. I am, however, trying to educate the members of my staff to realize the importance of recognizing the clinical signs suggestive of impaired metabolism or other physical derangements, and I am relying more and more upon their discretion to determine which patients need certain tests. In the case of the dispensary patient who is to enter the ward, I have the necessary examinations made before admission to the hospital.

I do not agree with the gentleman who says that patients demand immediate operation. It is really easier to persuade those who need operation to enter the hospital after the clinic worker has established a personal contact with them, for which a week or two of palliative treatment is usually required.

I have also found that the private patient will not object to necessary diagnostic procedures if I explain that these things are done solely for her own protection.

I agree that it is not advisable to carry out any elaborate diagnostic measures without some definite indication, but if we develop our powers of observation and seize the clues which the general physical make-up of the patient very often suggests, the selection of the proper tests becomes a simple matter.

Some years ago Dr. Baldy, of Philadelphia, reported a series of 3,413 gynecologic operations in which 16 sudden postoperative deaths occurred. The most striking feature was that 13 of them occurred in 366 cases of hysterectomy for fibroid, leaving 3 in 3,047 operations for other conditions. Unfortunately, I have not been able to determine the total number of pelvic operations that I have done personally, but I know that since 1915 I have had but two sudden postoperative deaths, one of which was due to acute paralytic ileus and the other to pulmonary embolism following a thrombosis in the femoral vein.

**DR. S. H. GEIST** read a paper entitled: **Study of Basal Metabolism and Weight Following Bilateral Oophorectomy.** (See page 206.)

#### DISCUSSION

**DR. M. A. GOLDBERGER.**—The period of observation was carried out only for from three to five months postoperative, but we are continuing our studies in these cases in a special follow-up clinic, where we are studying not only operatively castrated women, but also women who have been subjected to x-ray and normal menopause. These cases are to be followed for a period of about two years and will be reported upon later.

The second important fact in our paper is that in  $\frac{1}{3}$  of our cases there is a diminution in the basal metabolism with an increase in weight. This rather coincides with most of the experimental work which has been done on animals, especially that of Murlin and Bailey.

The third fact is that the weight increase in animal experimentations might be explained by the recent work of Wang and independently by Slonaker, who showed that when albino rats were placed in activity cages there was an increase in activity every four days. This corresponds to the estral cycle of an albino rat. In the interestrus, during pregnancy, and in senility there is a marked fall, but the fall is most marked in castrated rats, being as much as 90 per cent. This may explain the increase in weight in most of the animal experimentations.

**DR. HAROLD BAILEY.**—It seems to me that the subject has practical import. If we are able to show changes not only in the lowered metabolism but in weight and activity as well, we should feel that there is a specific action of the ovary affecting the general metabolism of the individual.

Each of the two animals that we studied showed an increase in weight and a lowered metabolism of over 14 per cent, one being 14.2 and the other 17.6 per cent. They were animals of different size and they varied considerably in weight. If we cast out the gain in fat, which plays a negative part in metabolism, we still have one animal showing a 12 per cent and the other a 6 per cent lowering. Therefore it appears to be evident that in these two animals there was a specific reaction. It is a fact, however, that the animals became fond of us and we of them, and there is no question that following the operation they became more inactive, and it is highly probable that this inactivity and friendship between animals and man had something to do with the change in the other experiments. In other words the dogs lay more quietly throughout their detention in the metabolism apparatus. If we consider this as an important point, we must admit that we have not produced conclusive evidence of specific reaction, especially as we had only two animals. The thyroid raises the metabolism in castrated animals, and our results with the dog that had no thyroid acted as a control for the other dog. It was to be expected that the metabolism in the dog without the thyroid would suffer a considerably greater reduction, but this was not the fact; the reverse was true, for the animal with the intact thyroid suffered a diminution in its total metabolism much greater than the other.

Dr. Geist's results show, according to the figures on the charts, an increase in weight in over 50 per cent of the cases and a lowered metabolism in 62 per cent. This percentage is not high enough to term the reaction specific, but it seems to me that it shows the probability of a general change, providing that all these women were in the active sexual stage.

I cannot but feel that there is common sense back of our contention. It is expected by lay persons that a woman will gain in weight after the menopause just as it is expected that a young woman after puberty will gain the contours of a woman's figure, and, moreover, food animals are commonly castrated in order that they may gain in weight. It would have been interesting if we could have followed our animals and found that the changes were the same a year later; and likewise Dr. Geist's patients should be examined after a considerable period.

I confess that I cannot feel that this presentation depreciates the work of Loewe and Richter and others; I think it substantiates it.

DR. ROBERT T. FRANK.—The material which the doctor has presented shows the enormous amount of work involved in such a research. It has taken the co-operation of four workers to cover this field. Forty-eight cases studied in this thorough fashion are a tremendous number, and yet with this large number upon which to base his statistics, you will notice that no absolutely striking conclusions could be reached. What does that mean? If you take the lower animals, for example, the queen bee, you will find that the entire life of the female is occupied with one thing, the sexual function. If you take the rodents which Dr. Goldberger mentioned, studied in the activity stage, a tremendous difference between the sexually quiescent period and the active period brought on by estrus, is very striking; when you take Dr. Bailey's dogs, it will be noted that there is a distinct diminution of this fluctuation due to the sex cycle, and when you come to the woman the sex phase plays a comparatively minor rôle as compared with the lower species. The fluctuation, to my mind, gradually diminishes, and, therefore, if it is traced from where it is most marked as in the bee, to the higher primates, a progressive diminution of the ovarian effect, as far as these extragenital phenomena are concerned, seems to obtain. That, however, does not mean that the ovary does not play a tremendous rôle in the primate.

My suggestion would be for Dr. Bailey to interest the physiologists in the chimi-

panzee and to practice on the monkey the same experiments that he had to give up in the dog.

I think Dr. Geist's conclusions that the removal of the ovary does not produce sufficiently striking symptoms to necessitate leaving it behind, if there are strong technical reasons for removing it, do apply. I think he is correct in his deduction. Possibly, if we can develop a more accurate technic of obtaining the basal metabolism, eliminating the huge technical error which must be allowed for, as normal, of 15+ to 15- per cent, his results will become more striking.

The main conclusion that is justified from this paper is that the folklore, more or less accepted by the medical profession of today, that tragic consequences must follow removal of the ovary, is greatly exaggerated.

DR. I. C. RUBIN.—I think one obstacle in the scientific study of this subject will always be the fact that we practically never castrate *per se*. In other words, the patients who were operated upon in Dr. Geist's series were operated upon either for the removal of large fibroids or double disease of the adnexa. You cannot deduct inferences from the lower animals in the human sphere for the reason that you can take out or leave at will ovaries in the dog or the rodent, and you cannot do that in the human species. So far we do not know anything with any degree of scientific certainty about metabolism following bilateral oophorectomy beyond the one point of the gain in weight, which is only a small detail. It is perfectly natural for women to bleed a good deal from fibroids and disease of the adnexa for the relief of which operative removal of the genitals becomes imperative. The ovaries in Dr. Geist's series were incidentally removed with the uterus. The relief from the drain entailed for months by the blood loss itself is followed by a gain in weight without necessarily ascribing this increase in weight to the fact that the ovaries had been removed. This and a certain possible psychic relief that comes from the knowledge of being rid of disease are factors that cannot be translated from the lower animals to the highest primates.

We also do not know whether or not the uterus *per se* has any effect upon metabolism and you will have to have a series of control cases, for example where the uterus is left *in situ* and check them up with all the painstaking detail that Dr. Geist and Dr. Goldberger have done in their present report.

While the effort is absolutely a worthy and creditable one, we shall always have this difficulty to deal with in working upon the matter of basal metabolism following hysterectomy in contradistinction to animal castration.

DR. J. A. CORSCADEN.—We have brought about radium castration, so-called, that is, cessation of menstruation with the appearance of hot flashes, which seems to be the criterion of the established menopause, in some 200 women, in whom there was an average gain in weight of 8 pounds. I think Dr. Rubin's stressing of the point that the fact that these women were diseased is important. Unfortunately, we have not controlled our cases with a lot of other similarly severe operations. It is very difficult to get general surgical conditions to compare exactly with these operations in the pelvis which require excision, but as far as superficial results go there is just about as much gain in weight in women operated upon for other conditions which do not involve the removal of the ovaries.

The second point is that in our studies of basal metabolism we have 11 women who have gone two years and in these the basal metabolism figures have persisted. We have two cases which are interesting. One is a woman who was made amenorrheic by radium when the basal metabolism was -17, and it has persisted at that point; it has not varied above or below during the two years. The other case was one of exophthalmic goiter, whose bad condition demanded the amenorrhea. Her basal metabolism was 20+ and still persists at the end of about two years.

DR. GEIST (closing).—One fact is certain; there is a gain in weight and a diminution in basal metabolism following castration. Whether or not the castration as an operative procedure causes these changes or whether some disturbance resulting from the removal of the ovaries does it, I cannot at the present time state.

To answer Dr. Rubin's query concerning the removal of the ovaries and the question of preexisting disease having an influence; we can state that we are now studying the same factors in women in whom the menopause is normal, where the effect of disease and the removal of the ovaries does not enter into the question. Possibly at a later date we shall be able to clear up this particular phase.

As to the question raised relative to a gain in weight because of the removal of diseased organs, it is interesting to note that in six of these women the weight was between 190 and 210 pounds, that they were suffering from local conditions, and did not present any general disease. One could readily conclude, therefore, that no general debilitated condition caused a change in their weight and basal metabolism.

It would be important if some one would undertake the same study on general surgical cases to see what effect the removal of the gall bladder, kidney, etc., would have upon the subsequent course of basal metabolism or weight. Dr. Corseaden mentioned the fact that he had a case whose basal metabolism remained at -17 and varied very little after castration. We too have had a number of similar cases that showed, following castration, no change at all. It must be remembered, however, that in a large number there was a tendency toward diminution in basal metabolic rate. As I mentioned at the outset of the discussion, whether these variations are due to some extraneous factors or to defects in our clinical methods of investigation, as Dr. Frank also mentioned, is a question which, at the present time, cannot be answered definitely. There is a possibility that they are simply accidental findings and, on the other hand, we have been unable to prove that the results may not be due to some functional change which results when the ovaries have been removed.

#### BROOKLYN GYNECOLOGICAL SOCIETY

STATED MEETING, MARCH, 1926

DR. WM. P. GRAVES, of Boston, read, by invitation, a paper entitled, **Problems of Organ Conservation in Pelvic Surgery.** (See page 217.)

#### DISCUSSION

DR. JOHN O. POLAK.—I wish to state that on the question of supracervical *versus* total hysterectomy, I have modified my views. I have been doing total hysterectomies for a number of years and have perfected a technic that is very satisfactory, but I am free to say that supracervical hysterectomies are very much more easily and quickly performed and my patients make a smoother convalescence, although the mortality is very little different in the two types of operation. I now do complete hysterectomies only in those cases where there is extensive disease of the cervix, complicating the pathology of the uterus for which the operation is done. I am forced to conclude that my mortalities and morbidities are slightly lower than they were when I was so enthusiastic about panhysterectomies.

That cervical cancer is a definite entity and does occur in the retained stump, Dr. Graves admits, but I am now taking care of the cervix prior to operation, with the cautery and tracheloplasty, depending on the microscope for subsequent treatment.

With radium we have a method of treatment for these cervices that are left. In suspicious cases we can absolutely eliminate the occurrence of cancer by using radium on the stump.

The question of conservation of the uterus and of the ovaries in various types of pelvic disease is indeed controvertible, and in this I disagree with Dr. Graves, as I find that the woman's psychic life is taken up with two thoughts: will I menstruate? and if I do not, why not? In other words she is spending her life in expectancy and disappointment and that is what unstabilizes our women. I feel that if we are going to do conservative pelvic surgery we should try to preserve the menstrual function. This is indeed most necessary in young women, where an ovary can be conserved. On the other hand, if the ovaries have to be removed then I believe that it is better to remove everything. In the conservation of ovaries, etc., in young women, affected by extensive inflammatory disease, where conservative surgery is practiced, further operative procedure may have to be undertaken.

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

## Collective Review

### New Books

BY ROBERT T. FRANK, A.M., M.D., F.A.C.S., NEW YORK CITY

OF GENERAL interest to the medical profession are two quite dissimilar volumes, the first a purely objective exposition dealing with the physiology of sex, the second a highly speculative structure which treats of the origin of life.

In many ways Marshall's short *Introduction to Sexual Physiology*<sup>1</sup> is more satisfactory than its larger predecessor *Physiology of Reproduction*. This is, perhaps, due to the fact that the necessity for compression has forced Marshall to feature his own opinions to a greater extent. The book is meant especially for the student of biology, medicine and agriculture, but really carries a far wider appeal. The addition of such subjects as abortion, rate of propagation and birth rate in man is commendable, as also is the discussion of such fanciful topics as *Zenith* and maternal impressions, if only to lay their ghost.

In my opinion the rapid advance of our knowledge of the causes of sex phenomena will soon permit far greater simplification in the discussion of the forces at work, and of the chemical basis of sex. Marshall is fully justified, however, while writing such a guide, to incorporate only the fully accepted and worked-out phases of the subject and to leave the most recent acquirements for a future revision.

No pathologist will agree with Marshall that "When the tissue denudation (of the uterine mucosa) is exceptionally great the condition is known as menorrhagia \* \* \* " (p. 52). The explanation of excessive menstrual bleeding is not quite so simple as that! The modern students of sex physiology are more and more abandoning the view that the normal nutritional condition of the uterus is influenced largely by the interstitial cells, though Marshall appears somewhat hazy in his analysis of nidation. He recognizes on the one hand that the corpus luteum prepares the uterine mucosa for reception of the ovum, but does not appreciate that Leo Loeb's work on artificial "deciduomata" or "placentomata" (which he mentions) demonstrates that nidation (certainly among rodents) is dependent upon that special function of the yellow body which governs the formation of the maternal part of the placenta. That the corpus luteum can be dispensed with early in pregnancy is fully explained by the vicarious action of the chorion and placenta.

Marshall's book is to be recommended highly to all medical men.

George W. Crile,<sup>2</sup> together with Amy F. Rowland, has put into book form the conclusions to which his various studies in different fields, but all directed toward the same end, have led him. Summed

<sup>1</sup>An *Introduction to Sexual Physiology. For Biological, Medical and Agricultural Students.* By F. H. A. Marshall, F. R. S., Longmans, Green, and Co., London, 1925.

<sup>2</sup>A *Bipolar Theory of Living Processes.* By George W. Crile, Edited by Amy F. Rowland, Macmillan Co., New York, 1926.

up, the author believes that all life is ascribable to a bipolar condition. Starting with the atom and ending with man as the highest primate, he tries to prove the uniformity of the bipolar pattern. To use the author's own words, "The purpose of this thesis has been to present certain evidence and deductions based upon that evidence in support of the theory that man and animals are bipolar mechanisms and that the organism not only is driven by electricity, but that it was originally created and constructed by electrical forces."

In substantiation of this highly interesting and speculative hypothesis, Crile draws all the evidence adducible from his own many researches and from those in the literature. It will take the work of many physiologists, both critical and constructive, to prove or disprove the tremendous amount of material, not all of which has hitherto been accepted by physiologists, in order to arrive at a more final conclusion.

#### GYNECOLOGY

The excellent impression made by the first edition of Schröder's *Textbook of Gynecology*<sup>3</sup> (reviewed in 1923) is fully confirmed by the present second edition in which the general form of the first edition has been retained, but numerous improvements have been made. Especially commendable are the added colored illustrations of microscopic specimens. The criticism, made in the previous edition, that Schröder had entirely overlooked the American literature no longer applies, as the author has made a serious attempt to credit American authors for the work done in the last years. The book shows such originality in dealing with modern problems of gynecology that a translation into the English language would be fully warranted, as we have no English textbook which gives as conservative and modern an exposition as this one.

Not less than seven large installments of Halban and Seitz's *Biology and Pathology of the Female*<sup>4</sup> have arrived since the last review. These include installment 18 to 24 and cover an enormous amount of ground. Installment 18 deals with the *normal and pathologic conditions of the placenta and the amniotic fluid* by Hans Hinselmann. This work is particularly striking because of the profuseness and excellency of the illustrations. The literary references are most difficult to examine as many of them are not even alphabetically arranged and, as in the rest of this series, are far from complete. H. R. Schmidt has dealt with the *pathology of the decidua, the membranes and the cord*.

Installment 19 contains the *physical chemistry of pregnancy, labor and the puerperium* (H. Schade). He describes such changes as occur because of the presence within the uterus of a new focus of intense metabolism, comparable in some way to the metabolic changes resulting from inflammation.

The *physiology of pregnancy* is taken up by E. Kehrer. He believes that ovulation does not occur during pregnancy. He recognizes the paramount importance of the corpus luteum during gestation but has not incorporated the newest discoveries in his discussion. The blood and metabolic changes of pregnancy are satisfactorily discussed.

In installment 20 Eufinger has been assigned the chapter on the *diag-*

<sup>3</sup>**Lehrbuch der Gynaekologie fuer Studierende und Aerzte.** By Dr. Med. Robert Schröder, Verlag von F. C. W. Vogel, Leipzig, 1926.

<sup>4</sup>**Biologie und Pathologie des Weibes.** By Prof. Josef Halban, Wien, und Prof. Ludwig Seitz, Frankfurt, a.M. Lieferung 18, 19, 20, 21, 22, 23, 24, Urban and Schwarzenberg, Berlin, 1925.

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nosis of pregnancy. Guggisberg devotes more than 200 pages to *labor pains*. I note that no mention of Dixon's theory of the initiation of labor through pituitary hypersecretion is mentioned, although many of the other theories have received comment. Pathologic contractions are discussed in great detail.

Installment 21 by A. Mayer covers the subject of the *clinical aspects of ovarian tumors* in a satisfactory fashion. An enormous bibliography covering 60 full pages of close print concludes this chapter, but, unless the reader wades through this tremendous material, author by author, the references to the literature are of no particular value. In the same installment Füth has described *injuries and foreign bodies in the genital tract*. Included in his exposition are the injuries resulting from childbirth.

Installment 22 contains the *diseases of the peritoneum* by Karl Baisch. He believes that well developed, diffuse bacterial peritonitis is a strictly surgical disease, recommending median incision, evacuation of the pus, followed by irrigation, wiping out of the purulent exudate, counter incision, and tube drainage. If the cause can be dealt with readily, he advises that this be done. I find no new statistics available. The author takes no very decided stand on the treatment of tuberculous peritonitis, describing impartially surgical, medical and roentgenologic therapy.

To v. Jaschke has been assigned the discussion of the *female breast*.

Installments 23 and 24 contain *operative obstetrics* from the pen of that dean of gynecology, Winter of Königsberg. Before dealing with the operative technic, the author discusses most thoroughly the indications for interruption of pregnancy or the induction of labor. He employs a tongue-shaped incision on the cervix and anterior vaginal wall as the first step in anterior vaginal hysterotomy. He has given up entirely the use of the Bossi dilator in favor of more surgical methods. According to him, vaginal cesarean section is the sovereign method of dilatation. His stand on episiotomy is conservative. This procedure should not be considered the typical method of preserving the perineum. He limits the applicability of hebosteotomy to multiparae. The *Kielland forceps* is discussed by Dr. Karl Fink as a subsidiary portion of this chapter. He considers the new forceps as a valuable instrument, particularly with a head high up in the pelvis but believes that it requires large obstetric experience to distinguish the cases in which this instrument is particularly indicated. In lower positions of the head, the Kielland forceps offers no advantage over the standard methods.

As regards cesarean section, the classical cesarean, as well as the transperitoneal method of Doederlein and Krönig, are emphasized. The flap operations current in this country are merely mentioned. On the whole, this exposition of operative obstetrics is most satisfactory.

#### OBSTETRICS

Ehrenfest has given us an American edition of *The Therapy of Puerperal Fever*,<sup>5</sup> written by Robert Kochler. This is the first work dealing specifically with puerperal infections that has been available to the English speaking physician for many years. The work covers

**Therapy of Puerperal Fever.** By Dr. Robert Kochler, Vienna. American Edition prepared by Dr. Hugo Ehrenfest, St. Louis, The C. V. Mosby Co., St. Louis, 1925.

the entire field most thoroughly, beginning with protection of the patient before and during labor and deals with prophylactic immunization, which the authors agree is not feasible for general application.

Part II is devoted to therapy. The respective chapters are divided into *General Therapy*, *Local Therapy*, *Surgical Therapy*, *Medicinal Treatment of General Infection*, and *Chemotherapy*. The entire literature is gone into in considerable detail. On the whole, like all others, the authors find our efforts to combat the infection by radical means most unsatisfactory. This applies to surgical treatment, including ligation of the veins, as well as to chemotherapy (foreign protein, dyes).

This book is recommended to the entire profession as a valuable and entirely unbiased presentation of what we know of the subject. This is quite in contrast to the next volume to be discussed.

*Geddes*<sup>6</sup> has given us a biased exposition of *Puerperal Septicemia: Its Causation, Symptoms, Prevention and Treatment* in a book which received the Nicholls prize in 1924 from the Royal Society of Medicine. This rather voluminous monograph boils down to the following (after one has waded through literature of bacteriology, etiology, and influence of climate and other conditions): that industrial accidents determine the puerperal fever rate in every district because such accidents invariably cause septic wounds. The resulting septic wounds become sources of infection to women in labor through the agency of the medical practitioners, because these latter cannot avoid being contaminated by such wounds in their daily practice. Nothing in the tedious mass of statistics, through which I found it necessary to wade, throws any new light upon the subject. The author's desire to have obstetric cases attended by qualified specialists in proper hospital environment is naturally devoutly to be sought for irrespective as to whether we accept his deductions or not.

*Dorland and Hubeny*<sup>7</sup> have published an *atlas of x-ray in embryology and obstetrics*. This compilation covers the x-ray findings on both the fetus and the adult and therefore the title is somewhat misleading.

The biologic effect of the x-ray is thoroughly detailed. Injury to the fetus in utero, due to raying, is fully reviewed. The authors mention that the bone centers, as demonstrated by clearing oils, and those shown by the x-ray do not correspond; that ossification is more rapid in the female; and that the first site of ossification demonstrable is in the region of the incisor tooth of the inferior maxilla, which can be demonstrated at the seventh week. Anomalies of skeletal development are fully discussed. Viseeral anomalies, especially displacements, as seen in the newborn, are of interest. A large part of the volume is devoted to x-ray of the female pelvis and its employment in determining bony contracture. The concluding portion of the book deals with teratologic radiography. A large bibliography concludes each chapter. Numerous plates illustrate the text.

*Modern Views on the Toxemias of Pregnancy* by *de Wesselow and Wyatt*<sup>8</sup> appears in the *Modern Medical Monographs* edited by *Hugh*

<sup>6</sup>*Puerperal Septicemia: Its Causation, Symptoms, Prevention and Treatment*. By George Geddes, M.D., C.M., Wm. Wood and Co., New York, 1925.

<sup>7</sup>*The X-Ray in Embryology and Obstetrics*. By Dr. W. A. Newman Dorland and Dr. M. J. Hubeny, Bruce Publishing Co., St. Paul, Minn., 1926.

<sup>8</sup>*Modern Views on the Toxemias of Pregnancy*. By O. L. V. de Wesselow and J. M. Wyatt, Paul B. Hoeber, Inc., New York, 1925.

*Maclean.* Although the views expressed are modern, the book itself was written before June, 1923, not appearing in print until 1925. Like others of the series, it is intended for the general practitioner. To be commended is the emphasizing of Stroganoff's treatment of eclampsia which, it is hoped, will more and more replace the radical procedures, except in very rare and selected cases.

Bourne in his *Recent Advances in Obstetrics and Gynecology*<sup>9</sup> tries to record the trends of opinion and movements of thought which have really affected medical practice for some time. The large field can naturally be covered only in a fragmentary way, but the author has shown good judgment in concentrating upon important problems and in giving them adequate discussion.

He emphasizes the fact that the tendency in the treatment of eclampsia is more and more toward conservative measures, the Stroganoff method or some modification of it being most in favor. He mentions a treatment for placenta previa, devised by Willet, in which a traction clamp connected with a weight attached to the bed is applied to the fetal scalp, thus not only hastening labor, but producing continuous pressure on the placenta.

Bourne speaks most glowingly of Fothergill of Manchester's technique in the cure of prolapse. He misses an excellent opportunity in his discussion of the ductless glands by not mentioning any of the more recent advances in the knowledge of the function of the ovary. On the other hand I prefer his entirely agnostic point of view to that of the uneritical "endoerinologist." In discussing Sampson's chocolate cysts, he emphasizes Bailey's work, which is hardly known in this country. Special chapters are devoted to *electrotherapeutics in gynecology* (written by Justina Wilson) and *radium in the treatment of carcinoma of the cervix* (written by Malcolm Donaldson). The appendix contains some instruments of which only the Bonney ligature reel appealed to me. This résumé is far superior to some of the year books regularly published.

Spencer<sup>10</sup> has written a scholarly brochure on *cesarean section*. It is based on 120 personal cases with a maternal mortality of 3.3 per cent, an immediate fetal mortality of 4.1 per cent, and a total infant mortality of 10 per cent. The author emphasizes that cesarean section is too frequently performed at the present time. Some reproductions of quaint woodcuts from ancient manuscripts add to the interest of the volume.

The second edition of Dr. Brodhead's<sup>11</sup> little book on *Approaching Motherhood* has just appeared. It is presented in the form of questions and answers in order to simplify its use by the expectant mother. The advice given appears sound throughout and is presented in a readable form.

De Cotret<sup>12</sup> has written a short elementary compend for the obstetric nurse, which has little to differentiate it from the many similar books on the market. This compend is evidently designed for the French-speaking portion of Canada.

<sup>9</sup>*Recent Advances in Obstetrics and Gynecology.* By Aleck W. Bourne, F.R.C.S., P. Blakiston's Son and Co., Philadelphia, 1926.

<sup>10</sup>*Caesarean Section, With a Table of 120 Cases.* By H. R. Spencer, M.D., William Wood and Co., New York, 1926.

<sup>11</sup>*Approaching Motherhood.* By George L. Brodhead, Ed. 2. Paul B. Hoeber, Inc., New York, 1925.

<sup>12</sup>*L'Obstétrique des Gardes-Malades.* By E. A. René de Cotret, Montreal, 1925.

We have also just received another of De Cotret's<sup>13</sup> books, published seven years ago, also in French, dealing with normal and pathologic puerperal conditions.

Eberhart<sup>14</sup> is the author of a short pocket compend on obstetrics for the young and inexperienced physician who occasionally turns towards obstetrics.

#### MISCELLANEOUS

J. Shelton Horsley's<sup>15</sup> *Operative Surgery* is unique in that it subordinates the purely technical descriptions to the physiologic result to be expected and obtained by operative procedure.

This second edition has incorporated Costain's lymphaticostomy for septic peritonitis, Stookey's operation for innervating paralyzed muscles, Finney's pylorectomy, Graham's pulmonary pneumectomy, and Cutler's valvotomy for mitral stenosis, as well as such other new operations as those for angina pectoris, and the method for intestinal resection devised by Kerr. The fact that Horsley has abandoned his own technic in favor of Kerr's, speaks highly for the author's open-mindedness, which is shown throughout the text.

For the reader interested in dealing not only with purely technical methods but also desiring to appreciate the underlying principles, the recognition of which differentiates a mere technician from a true surgeon, this book is to be recommended highly.

A magnificent *atlas of operative cystoscopy* comes from the pen of Ryall<sup>16</sup> of London. It covers the entire subject of technic as applied to this branch of examination, including anesthesia, the treatment of ureteral stone, dilatation of the orifice of the ureter, litholapaxy, as well as the removal of foreign bodies from the bladder. The treatment of bladder tumors is dealt with, as well as the use of diathermy and other methods in the treatment of prostatic diseases. The appendix describes the author's universal cystourethroscope. The main bulk of this impressive volume is taken up by the 115 wonderful plates, the greater majority of which are in colors and represent cystoscopic pictures drawn from nature. These cystoscopic pictures illustrate almost every conceivable condition in a lifelike manner. The legends appear in three languages, English, French, and German, so as to be readily used by readers of different nationalities. Of particular interest are the pictures taken in succession of the change in appearance of different conditions as the result of treatment or of the progress of a condition, for instance, such as is shown on Plate 12, beginning with the periureteral, bulbous edema resulting from the presence of an intramural stone; the appearance of the same ureteral orifice seven days later when the stone is just beginning to be born into the bladder; the subsequent appearance immediately following the application of diathermy, and finally a picture of the stone after expulsion. Illustrations of cystoscopic instruments in situ during, for example, the incision of a ureteral opening for the release of an impacted stone, might be mentioned.

<sup>13</sup>*Suites de Couches Normales et Pathologiques.* By E. A. René de Cotret, Montreal. La Cle D'Imprimerie Godin, Ltée, 1919.

<sup>14</sup>*Geburtshilfliches Brevier für Aerzte und Studierende.* By Dr. Franz Eberhart, Urban und Schwarzenberg, Berlin, 1925.

<sup>15</sup>*Operative Surgery.* By J. Shelton Horsley, M.D., Ed. 2, C. V. Mosby Co., St. Louis, 1924.

<sup>16</sup>*Operative Cystoscopy.* By E. C. Ryall, F.R.C.S., C. V. Mosby Co., St. Louis, 1925.

This atlas should prove of the utmost use, particularly to those who have not had the opportunity to become familiar with intravascular conditions from a large material. A welcome addition would have been an index of the plates.

A most interesting symposium covering the facts and responsibilities of birth control has been edited by Adolf Meyer.<sup>17</sup> The contributors are twelve in number, and all their contributions show a uniform standard of excellence. I think that the sentence written by Adolf Meyer in the preface, "Our primary concern is the development of a conscience concerning procreation," touches the keynote of the entire symposium. Dr. Meyer justly emphasizes the conservative (I might add ultraconservative) attitude of the medical profession toward birth control, a topic which is regularly excluded from textbooks, professional journals, and the curriculum of medical schools. The two bugbears most dreaded as an effect of this movement seem to be an undesirable spreading of promiscuity as well as the danger to the health of the participants.

The separate articles give a clear-cut, impartially presented and most gripping view of the entire problem from many aspects. Among the various topics emphasized, I might instance both physical and mental hygiene, the menace of overgrowth of population, the relation to public health, the ethical and social points of view, the biologic factor, and many other issues. The authors are representative in many fields: Adolf Meyer, psychiatrist at Johns Hopkins, Margaret Sanger, one of the main motive forces in this movement, C. C. Little, president of the University of Michigan, Raymond Pearl, the statistician, to mention only a few.

This little book should be read both by the friends and adversaries of the birth control movement, because both sides will profit by the impartial light thrown upon this important topic.

*Lynch and Felsen*<sup>18</sup> have written a book on the *pathology, diagnosis and treatment of tumors of the colon and rectum*. The anatomy is treated in a clear, if somewhat brief fashion. Chapter III, dealing with the pathology, is very satisfactory, because the authors have included a very brief clinical outline of the case, and it is always wise to contrast the pathology of the dead tissues directly with the clinical aspects of the condition. It appears to me that the authors might have added the outcome and result to these clinical briefs. The illustrations of the gross and microscopic conditions are satisfactory and instructive. I cannot praise the chapter dealing with the surgical treatment as highly, because, for example, in dealing with the perineal resection of the rectum, too many intermediate steps have been omitted, particularly in the illustrations, to make the exposition clear, especially to beginners. Another addition, which I hope will appear in future editions, will be an assembled table which gives the results obtained by the authors' personal experience with operations. The general make-up of the book is faultless and extremely attractive.

The twelfth edition of a very popular English textbook,<sup>19</sup> namely,

<sup>17</sup>**Birth Control, Facts and Responsibilities.** By Adolf Meyer, M.D., Williams and Wilkins Co., Baltimore, 1925.

<sup>18</sup>**Tumors of the Colon and Rectum. Their Pathology, Diagnosis and Treatment.** By J. M. Lynch, M.D., and J. Felsen, M.D., Paul B. Hoeber, Inc., New York, 1925.

<sup>19</sup>**The Diseases of Children.** By the late Sir James Frederic Goodhart. Edited by George Frederic Still, M.D., F.R.C.P., Ed. 12, Lea and Febiger, Philadelphia, 1926.

that originally written by the late Sir James Frederic Goodhart and now edited by George F. Still, appears five years after its predecessor. The editor has attempted to retain the flavor imparted by the senior author but has tried to incorporate the newest acquirements, such as, lymphadenoma, encephalitis lethargica, the Schick test, the vitamines in connection with rickets and scurvy, and similar topics.

*International Clinics*,<sup>20</sup> as usual, covers a large group of subjects, only a few of which are of immediate interest to the gynecologist and obstetrician. *G. P. Laroque* reports 1,000 consecutive cases of *appendicitis* operated upon by himself. Of these, 830 were clean cases (mortality of 0.5 per cent). The entire mortality for the series was 2.1 per cent. The large number of clean cases makes the critical reviewer wonder how many of these were benefited by operation. *C. Jeff Miller* has contributed a timely article on the *contraindications to the use of radium in gynecology*. The article by *N. B. Gwyn* on *Massive Collapse of the Lungs* is of most interest where referring to the postoperative occurrence of this rare complication.

*Nephritis* by *Elwyn*<sup>21</sup> gives a comprehensive presentation of some of the modern theories dealing with diseases of the kidney. It covers the physiology of this organ, renal insufficiency, uremia, and the as yet unsatisfactory classification of nephritis. He explains the pathology and clinical changes occurring in the course of pregnancy, on the basis of a general arterial contraction from the beginning of pregnancy. The author assumes that there is a purposive mechanism consisting of an increased irritability of the pregnant uterus, as well as that of the entire neuromuscular mechanism, which has to do with the function of uterine contraction, in that this mechanism results from a similar hypersensitivity of the presiding centers in the brain. In certain cases the other vegetative centers in the brain, especially those dealing with vasoconstriction, which are closely adjacent, are likewise affected. He believes that an external stimulation to this vasoconstriction apparatus may be due to the hemolysis caused by the incompatibility between the blood of the child and that of the mother. This highly speculative hypothesis does not appear to be borne out, in my opinion, by such clinical data as have accumulated up to this time. A valuable bibliography will be found at the end of each chapter.

This little manual,<sup>22</sup> printed on extremely thin paper so as to occupy a small compass, consists of three hundred sixty-one pages of text. It covers the treatment of dangerous hemorrhages occurring in pulmonary, cardiae, nervous, gastrointestinal and renal systems, also obstetric hemorrhages, as well as poisonings. This rather heterogeneous conglomeration is fairly well handled. The treatment is based upon Lenzmann's books and schematization. This book may prove of value to those unexpectedly and unpreparedly confronted with emergencies.

*Drouet*<sup>23</sup> has issued a third edition of his treatment of syphilis by means of bismuth according to the methods used in Paris hospitals.

<sup>20</sup>*International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles.* Volume I. Thirty-sixth Series, 1926. J. B. Lippincott Co., Philadelphia and London, 1926.

<sup>21</sup>*Nephritis.* By H. Elwyn, M.D., The Macmillan Co., New York, 1926.

<sup>22</sup>*Manual of Emergencies.* By Dr. J. Snowman, William Wood and Co., New York, 1926.

<sup>23</sup>*Le Traitement de la Syphilis par le Bismuth.* By Dr. Georges Drouet, Ed. 3, A. Maloine et Fils, Paris, 1926.

He claims that bismuth treatment is indicated where intolerance or resistance to arsenicals is encountered.

Morison and Saint<sup>24</sup> have prepared this second edition of *An Introduction to Surgery*. The text consists of an elementary treatise for the medical student, covering the general principles underlying surgical diseases. The treatment of the subject is simple, clear, and direct. The chapter on natural cures is well worth careful perusal. This chapter deals mainly with biliary conditions. The final chapter dealing with pathologic conditions, illustrating the application of the general principles, is a good summary of the entire volume. The illustrations are good.

*Pygmalion or the Doctor of the Future*,<sup>25</sup> appearing in the *Today and Tomorrow Series*, is designed to demonstrate that a symptom need not necessarily be a sign of disease, that a given symptom may be but an "altered reaction to life occasioned by the presence of disease." The author makes his point cleverly and clearly.

Dickson's<sup>26</sup> presentation is a farrago of quotations, surmises, and assertions which do not deserve serious critique. "There is a distinct and separate hormone entity in the axillary and pectoral lobes (of the breast) respectively." Does he refer to the cow or the biped? We are glad to learn that imperforate hymen is not amenable to endocrine treatment. John Hunter should turn in his grave when his dictum "Don't think—try" is perverted to such ends. In his summary the author modestly disclaims "perfection for this work."

<sup>24</sup>**An Introduction to Surgery.** By Dr. R. Morison and Dr. C. F. M. Saint, Ed. 2, William Wood and Co., New York, 1925.

<sup>25</sup>**Pygmalion or the Doctor of the Future.** By R. M. Wilson, M.B., Ch.B., E. P. Dutton and Co., New York, 1926.

<sup>26</sup>**Rational Gland Therapy for Women, Particularly in Relation to Menstruation.** By I. Wanless Dickson, M.B., F.R.C.S., London, H. K. Lewis and Co., Ltd., 1926.

## Item

### A NEW DELIVERY BED\*

BY GEORGE GELLIHORN, M.D., F.A.C.S., ST. LOUIS, MO.

The delivery bed here presented possesses several distinctive features.

1. The footrests which commodiously incase the entire foot, are on a level with the bed. This means that, during the second stage, *the auxiliary musculature of the abdomen can come into play* far better than if the heels were suspended from upright leg holders or if the legs were held by attendants.

2. Conveniently shaped knee supports prevent fatigue. These and the footrests are easily adjusted to suit the size of the individual patient.

3. Washable straps around both the ankles and the knees effectually secure the legs in any desired position without excessive restraint, and render unnecessary the services of the two attendants who are usually needed for that purpose. In training schools, therefore, *nurses have an opportunity to watch the progress of labor rather than act as human leg holders*.

4. Shoulder braces, readily adjusted and well padded with spongy rubber, prevent the patient from moving her hips away from the edge of the bed. The patient thus lies, throughout the second stage, *in a perfectly natural, comfortable, and non-fatiguing position which she cannot change, even when only incompletely narcotized*.

\*Demonstrated at the meeting of the American Gynecological Society, Washington, D. C., May 4 to 6, 1925.

The thick and resilient mattress of spongy rubber (not shown in the photograph) adds to her comfort, and the natural flexion of her hips forestalls the severe strain upon the sacroiliac joints to which patients in labor are often subjected.

5. The absence of uncontrolled movements upon the part of the patient safeguards the disinfection of the external parts, which is frequently nullified in other styles of delivery beds, and *the aseptic draperies are never disturbed*.

6. *The vulva remains exposed to view at all times*, and the extent of exposure can always be regulated according to the requirements of the case.

7. The perineum is not overstretched as in any form of exaggerated lithotomy position; hence, *deep lacerations are less likely to occur* if the labor is conducted with sufficient obstetric skill.

8. An adjustable shelf beneath the buttocks provides a convenient resting place for the baby until the cord is severed, and a receptacle for instruments, should perineal repair be necessary.

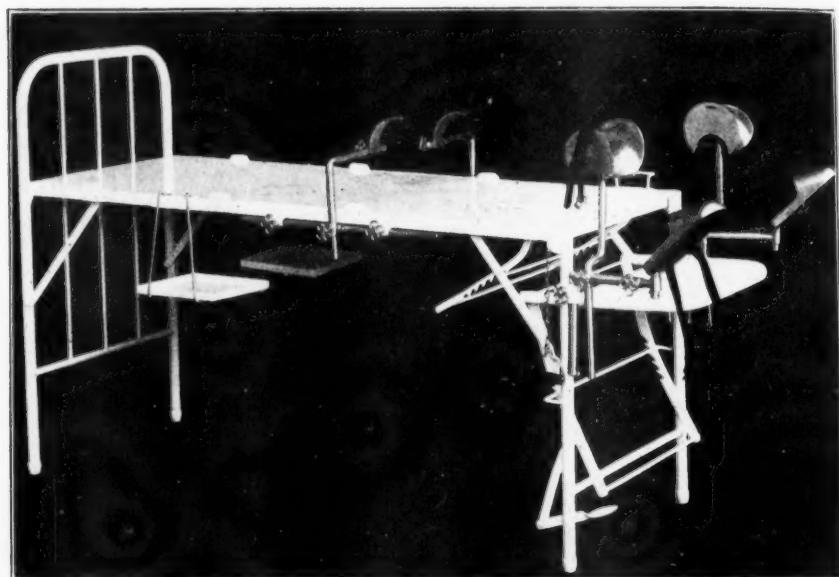


Fig. 1.

9. Provision is made to raise the pelvis for the few occasions where this would be desired (reposition of prolapsed cord, etc.).

10. Strong trays, firmly attached to the frame near the head end, serve for all appliances of the narcotizer and make additional furniture in the delivery room superfluous.

11. After narcosis is instituted, the hands of the patient may be secured in a leather sling (not provided with the bed), which excludes any interference from that source and enables the anesthetist to attend to his work without additional assistance. The nursing force is thereby eliminated as far as the maintenance of the patient's position is concerned—an obvious advantage, particularly in night deliveries.

12. The sturdy, yet extremely simple construction of the bed and its moderate price\* are further points of value.

METROPOLITAN BUILDING.

\*Built by the Smith-Davis Hospital Bed Company, St. Louis.